In the United States Court of Federal Claims

OFFICE OF SPECIAL MASTERS

No. 12-763V
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To be Published

DOUG AHLUM and KARI AHLUM, Parents and Next of Kin to T.A.,	*	
Petitioners,	*	
v.	*	Measles, mumps, rubella ("MMR") vaccine; systemic inflammatory response syndrome ("SIRS"); double amputation.
SECRETARY OF HEALTH AND HUMAN SERVICES,	*	
Respondent.	*	

Andrew D. Downing, Phoenix, AZ, for petitioners.
Debra A. Filteau Begley, Washington, DC, for respondent.

MILLMAN, Special Master

RULING ON ENTITLEMENT[1]

On November 9, 2012, petitioners filed a petition under the National Childhood Vaccine Injury Act, 42 U.S.C. § 300aa-10-34 (2012), alleging that measles, mumps, rubella ("MMR") vaccine administered to their son T.A. on August 11, 2011 caused him a Table encephalopathy. Pet. Preamble. T.A. was three years old at the time. Eleven days after MMR vaccination, T.A. was tired. Id. at ¶ 4. The following day, he had a 100-degree fever. Id. Thirteen days after his MMR vaccination, T.A. saw his pediatrician with a rash. Id. at ¶ 5. His red platelet count was low. That evening, T.A.'s condition worsened, his fever spiked at 103 degrees, and he had constant vomiting and diarrhea. Id. On August 25, 2011, 14 days after MMR vaccination, T.A. returned to his pediatrician. Id. at 6. His red platelet count was even lower and his white blood cells were very high. Id. He was put on antibiotics and hospitalized. His legs were amputated, at first below the knees, and then above the knees, to save his life. Petitioners' affidavits are consistent with their petition. Exs. 1 and 2.

[1] Vaccine Rule 18(b) states that all decisions of the special masters will be made available to the public unless they contain trade secrets or commercial or financial information that is privileged and confidential, or medical or similar information whose disclosure would constitute a clearly unwarranted invasion of privacy. When such a decision is filed, petitioner has 14 days to identify and move to redact such information prior to the document's enclosure. If the special master, upon review, agrees that the identified material fits within the banned categories listed above, the special master shall redact such material from public access.

On March 7, 2013, the undersigned held the first telephonic status conference with counsel. Petitioners' counsel said respondent was amenable to settlement and petitioners had recently made a demand. Respondent's counsel stated respondent was trying to put a value on the case. Because the case was complex, respondent's counsel had hired a life care planner. Petitioners' counsel said that petitioners participated in Qualchoice in Arkansas. They did not have coverage for a period of time. T.A. was enrolled in ARKids, which is a type of Medicaid. Petitioners had very little unreimbursable medical expenses. Petitioners' counsel provided an itemized Medicaid lien to respondent. T.A.'s medical treatment was mostly at Shriner's which does not bill for services.

One year later, on March 7, 2014, the parties still had not settled and respondent requested petitioners file expert reports. Both parties subsequently filed expert reports.

On May 13, 2014, petitioner filed an amended petition, alleging a Table injury of encephalopathy and a Table injury of thrombocytopenic purpura leading to systemic inflammatory response syndrome ("SIRS"). Am. Pet. Preamble and ¶ 11.

One year later, on March 31, 2015, respondent's counsel said respondent might possibly settle for less than it would cost respondent to try the case. Petitioners' counsel said he would not recommend settling for less than costs. During a status conference on April 28, 2015, petitioners' counsel said his clients were interested in settling but wanted to know how far below litigative risk that amount would be. Respondent's counsel said she did not know if it made sense to settle. By June 3, 2015, it was apparent the parties would not settle.

The undersigned held a three-day hearing from March 1-3, 2016. On March 4, 2016, the undersigned issued an Order explaining the issues and encouraging settlement. During a status conference held on May 31, 2016, respondent's counsel said respondent was not amenable to settlement.

After considering all the evidence, including the experts' reports and medical literature upon which the experts relied, and the testimony of the parents, T.A.'s pediatrician, and the experts, the undersigned rules for petitioners on entitlement.

FACTS

Prevaccination Records

T.A. was born on March 10, 2008.

From July 25-30, 2008, T.A. was at Dell's Children's Medical Center of Central Texas for acute lymphadenitis[2] with a *Staphylococcus aureus* infection. Med. recs. Ex. 13, at 1. T.A.

[2] Lymphadenitis is inflammation of one or more lymph nodes." DORLAND'S ILLUSTRATED MEDICAL DICTIONARY 325 (32nd ed. 2012) [hereinafter "Dorland's"].

had presented with neck swelling and fever. Fluid collection was consistent with abscess. He had incision and drainage on July 27, 2008 and was put on antibiotics. Id. at 4.

On August 30, 2008, T.A. was taken to Mercy Hospital Northwest because of a neck abscess. Med. recs. Ex. 5, at 20. He was diagnosed with cellulitis and abscess of the neck. Id. He was discharged on September 3, 2008. Id. at 25. T.A. had a similar problem a month before in Austin and had to have an incision and drainage. Id. The current problem started less than one week earlier with gradual onset. Id. Incision and drainage were performed on September 1, 2008. Id. at 31. The prior neck abscess reportedly grew *Staphylococcus aureus*. Id. No organisms were detected with this neck abscess. Id. at 59.

On August 27, 2009, at 17 months, T.A.'s mother phoned the pediatrician to report that T.A. had a rash on his feet and bottom since the day before. Med. recs. Ex. 12, at 1.

On June 22, 2011, T.A. saw Dr. L. Barry Allen, his pediatrician, for fever, vomiting, and abdominal pain. Med. recs. Ex. 3, at 7. On physical examination, T.A. had possible early pharyngitis. There was some exudate on his tonsils. He also possibly had early cellulitis[3] of his eyes,[4] particularly his right eye. There was a scar over his right anterior cervical area from a previous abscess. His white blood count ("wbc") was normal. His platelet count was 144,000. Hemoglobin and hematocrit were low at 10.5 and 29. Dr. Allen was concerned about pharyngitis, possible early cellulitis. Id. Dr. Allen prescribed Augmentin[5] 600 and Moxeza[6] eye drops. Dr. Allen notes that T.A. had had anemia intermittently for at least three years. Id. The blood count from a couple of years ago showed anemia with hematocrit of 28 or 29. Id. at 7-8.

Postvaccination Records

On August 11, 2011, T.A. saw Dr. Allen for his three-year-old well child examination. Med. recs. Ex. 3, at 10. Dr. Allen wrote that T.A. had been doing well and had not had any trouble up to the present time. T.A. received MMR vaccine. Id.; Ex. 4, at 1.

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[3] Cellulitis is "an acute, diffuse, spreading, edematous, suppurative inflammation of the deep subcutaneous tissues and sometimes muscle, sometimes with absence formation. It is usually caused by infection of a wound, burn, or other cutaneous lesion by bacteria, especially group A streptococci and *Staphylococcus aureus*, but it may also occur in immunocompromised hosts or following erysipelas." Dorland's at 325. Erysipelas is "an acute superficial form of cellulitis involving the dermal lymphatics, usually caused by infection with group A streptococci. Characteristics include a peripherally spreading hot, bright red, edematous, brawny, infiltrated plaque with a circumscribed, raised, indurated border." Id. at 642.

[4] Facial cellulitis is "cellultis affecting the face, sometimes produced by spread of infection from nearby or distant foci. In children it is usually on just one cheek, and in adults it most often affects the neck; it may also occur around the eyes. It is tender, bluish in color, and poorly demarcated, with an edematous border, and patients often have fever, local pain, and bacteremia. *Haemophilus influenzae* type b, Group B streptococci, and *Streptococcus pneumoniae* are etiologic agents in young children." Dorland's at 326.

[5] Augmentin is "trademark for combination preparations of amoxicillin and clavulanate potassium." Dorland's at 179.

[6] Moxeza is also known as moxifloxacin hydrochloride, used "in the treatment of bacterial exacerbation" of illnesses caused by "gram-positive and gram-negative bacteria." Dorland's at 1184.

On August 24, 2011, 13 days after MMR vaccination, T.A. returned to Dr. Allen with fever. Med. recs. Ex. 3, at 11. The fever started the prior evening (August 23, 2011, 12 days after MMR vaccination). T.A. had a rash with fever of 102 degrees. T.A. had a petechial[7] rash, particularly on his neck and trunk. He had a macular[8] rash on his trunk as well. His tympanic membranes were dull, but normal. His throat was injected without exudates. His neck was supple, chest clear, abdomen soft, and his heart had a regular rhythm without murmurs. T.A.'s wbc was 6,000. His platelet[9] count was 97,000. Dr. Allen prescribed Rocephin[10] 750 mg intramuscularly ("IM") and would recheck T.A. on August 25, 2011, repeating his blood count that day. Id. According to Dr. Allen's lab results, T.A.'s wbc of 6,200 was within the normal range of 6,000-17,000. Id. at 12. T.A.'s platelet count of 97,000 was below the normal range of 150,000-450,000. Id.

On August 25, 2011, T.A. returned to Dr. Allen. Id. at 14. T.A. had vomiting and diarrhea during the night. On physical examination, Dr. Allen noted that T.A. was quite lethargic, and at least 10 percent dehydrated. His rash had increased. T.A.'s white count rose from 6,000 the day before to 20,000 that day. His neutrophil[11] count was 75% that day compared to 71% the day before. His hemoglobin was 19.6 with a hematocrit of 51.5, whereas the day before, his hemoglobin was 13 with a hematocrit of 35. T.A.'s platelet count that day was 73,000, whereas the day before it was 97,000. Dr. Allen assessed T.A. as being extremely dehydrated and toxic. He administered IV fluids and transferred him to the hospital for admission. Id.

On August 25, 2011, at 11:45 a.m., T.A. was brought to Mercy Hospital Northwest. Med. recs. Ex. 5, at 405. The history was decreased appetite, decreased activity, and fever. Id.

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[7] Petechia is "a pinpoint, nonraised, perfectly round, purplish red spot caused by intradermal or submucous hemorrhage." Dorland's at 1422.

[8] Macule is "a discolored skin lesion that is not elevated above the surface . . . ." Dorland's at 1094. "The typical [measles] rash consists of generalized maculopapular lesions that are at first discrete but gradually become confluent, starting behind the ears and on the face and progressing rapidly down the trunk and onto the extremities." Id. at 1116. Atypical measles is "a severe form of measles occurring after . . . in some cases live attenuated measles vaccine. It is characterized by fever, headache, myalgia, abdominal symptoms, and cough; this is followed by an atypical rash that may be urticarial, vesicular, petechial, or maculopapular, is found on the wrists and ankles, spreads to the palms, soles, and trunk, and later fades; there may be peripheral edema, interstitial pulmonary infiltrates, and pleural effusion. Koplik spots are absent." Id. "Being atypical, AMS [atypical measles syndrome] can be confused with other entities including Rocky Mountain spotted fever, meningococcal infection, various types of pneumonia, appendicitis, juvenile rheumatoid arthritis, etc." Medical Definition of Atypical measles syndrome (AMS), MEDICINENET, http://www.medicinenet.com/script/main/art.asp?articlekey=6619 (last visited July 19, 2018).

[9] Platelet is "a disk-shaped structure, 2-4 µm in diameter, found in the blood of all mammals and chiefly known for its role in blood coagulation. . . ." Dorland's at 1459.

[10] Rocephin is "trademark for a preparation of ceftriaxone sodium." Dorland's at 1651. Ceftriaxone sodium is "a semisynthetic, ß-lactamase-resistant, broad-spectrum, third-generation cephalosporin effective against a wide range of gram-positive and gram-negative bacteria; administered intravenously or intramuscularly." Id. at 312.

[11] Neutrophil is "a mature granular leukocyte that is polymorphonuclear (its nucleus having three to five lobes connected by slender threads of chromatin, and cytoplasm containing fine granules); neutrophils have the properties of chemotaxis, adherence to immune complexes, and phagocytosis." Dorland's at 1272. Leukocyte chemotaxis is "the response of leukocytes to products formed during an immune response, whereas leukocytes are attracted to and accumulate at the site of the reaction; it is part of the inflammatory response." Id. at 341.

at 410. Dr. Allen accompanied T.A. at the bedside and an IV was started. Id. Following stabilization, Arkansas Children's Hospital was called and T.A. was air lifted there. Id. at 427. Final diagnosis at Mercy Hospital Northwest was hyperglycemia, hyponatremia, ten percent dehydration, acidosis, and probable sepsis. Id. at 428. T.A. was given dopamine for blood pressure control and insulin. Id.

On August 26, 2011, Dr. Jose R. Romero did a consultation at Arkansas Children's Hospital. Med. recs. Ex. 7, at 473. The history was T.A. was in his usual state of health until Monday, August 22, 2011, when he felt tired. Id. On Tuesday, August 23, 2011, he woke with a temperature of 100 degrees. His mother gave him Tylenol and, after a nap in the late morning or early afternoon, his temperature was 104 degrees. On Wednesday, August 24, 2011, T.A. saw his pediatrician Dr. Allen at about 9:00 a.m. at which time his fever was 103 degrees. T.A. had a non-pruritic, pinpoint rash on his upper shoulders, back and slightly on his chest. Id. Dr. Allen told Dr. Romero that a blood culture was done, a nasopharyngeal swab was done, and a urine culture was done, and these were negative. Id. T.A. was given a dose of ceftriazone (Rocephin) and sent home. That evening, he vomited for an hour, slept fitfully, and developed diarrhea, which had no blood in it. Id. On Thursday, August 25, 2011, T.A. returned to Dr. Allen with lethargy. Id. at 474. Blood work showed an increased wbc. He was transferred immediately to the emergency room. Blood culture was drawn, which was negative. His IgG was 204. His C4 was low. About two weeks ago, he had swelling in Beaver Lake, but no one else was ill. He had tick exposure six weeks earlier. T.A. had a history of a separative lymphadenopathy in the neck at four months of age, which was drained, and a second episode which recurred about one and one-half months later, necessitating a second draining. Id. In addition he was at a fair and petted animals. On physical examination, T.A. had gross edema in his head, eyes, neck, and upper and lower extremities (and he was about to undergo dialysis). Id. T.A. had primarily a truncal petechia with good capillary refill. Id. at 474-75. T.A. had anemia. Id. at 475. His erythrocyte sedimentation rate ("ESR") and C-reactive protein ("CRP") were normal. His liver enzymes were normal. His platelet count was 55,000. He had evidence of disseminated intravascular coagulation ("DIC").[12] Dr. Romero's assessment was that T.A. had overwhelming sepsis,[13] thrombocytopenia,[14] DIC, and renal failure, was on Vancomycin (an antibiotic) although the level was low, and had low IgG, possibly hypogammaglobulinemia[15] or this could be due to illness. Id. Dr. Romero recommended changing the Rocephin to cefepime (another antibiotic), continuing Vancomycin, administering intravenous doxycycline (another antibiotic), doing blood and urine cultures, taking a Rocky Mountain Spotted Fever ("RMSF") titer, doing

[12] Disseminated or diffuse intravascular coagulation is "a bleeding disorder characterized by abnormal reduction in the elements involved in blood clotting due to their use in widespread intravascular clotting. It may be caused by any of numerous disorders; in the late stages, it is marked by profuse hemorrhaging." Dorland's at 376.
[13] Sepsis is "1. the presence in the blood or other tissues of pathogenic microorganisms or their toxins. 2. septicemia." Dorland's at 1693.
[14] Thrombocytopenia is "decrease in the number of platelets, such as in thrombocytopenic purpura." Dorland's at 1922.
[15] Hypogammaglobulinemia is "abnormally low levels of all classes of immunoglobulins in the blood; . . . ." Dorland's at 901.

an Ehrlichia[16] polymerase chain reaction ("PCR"), and doing a Tularemia[17] titer. Id.

Also on August 26, 2011, Dr. Susan Demirel took a history and physical. Id. at 533. T.A. was admitted to pediatric intensive care unit for shock. He had fever up to 102 degrees and a rash. Overnight, he had persistent vomiting and diarrhea. He was dehydrated and significantly more toxic appearing on the day of admission. The rash persisted. Chest x-ray showed a right middle lobe infiltrate. Id. On physical examination, T.A. had prominent scleral edema in his left eye. Id. at 534. His neck had adenopathy on the left. He had coarse breath sounds bilaterally with decreased breath sounds on the right. Id. His abdomen was taut and distended. Id. at 535. Dr. Demirel considered Kawasaki's[18] as a consideration in the differential diagnosis. Id.

On August 27, 2011, Dr. Richard J. Jackson did a surgical consultation. Id. at 477. T.A. had abdominal distension, possibly early abdominal compartment syndrome.[19] Dr. Jackson said T.A. had developed systemic inflammatory response syndrome ("SIRS") with diffuse capillary leak with increasing abdominal distension. Id. The etiology was not identified. All cultures were negative. T.A. remained thrombocytopenic. Id. Dr. Jackson decided not to perform surgery as T.A.'s intra-abdominal hypertension/compartment syndrome was not significant. Id. at 478.

Also on August 27, 2011, Dr. Mark J. Heulitt wrote a critical care medicine note. Id. at 486. T.A. had episodes of hypotension. The day before, he had some significant acidosis.[20] Id. His input and output were misbalanced. Id. at 487. T.A. had low platelets of 21,000 that morning. He continued with negative blood cultures and urine cultures. The antibiotics cefepime, doxycycline, and vancomycin were all adjusted for T.A.'s renal failure.

[16] Ehrlichia is "a genus of tick-borne bacteria. . . ." Dorland's at 596. Tests for Ehrlichia, *Staphylococcus aureus*, and *Streptococcus pneumoniae* were negative. Med. recs. Ex. 7, at 2239-41, 2274-75.

[17] Tularemia is "a plaguelike, zoonotic disease caused by infection with the bacillus *Francisella tularensis*, whose hosts include sheep and . . . rodents such as rabbits, squirrels, and muskrats. It is transmitted by the bites of deerflies, fleas, and ticks . . . and by ingestion of contaminated food or water. [M]ost cases are characterized by abrupt onset of fever, chills, weakness, headache, backache, and malaise." Dorland's at 1984.

[18] Kawasaki disease is "a syndrome of unknown etiology, usually affecting infants and young children, associated with vasculitis of the large coronary vessels and numerous other systemic signs, including fever, conjunctival injection, changes of the oropharyngeal mucosa, cervical lymphadenopathy, and maculoerythematous skin eruption that becomes confluent and bright red in a glove-and-sock distribution; the skin becomes indurated and edematous and often desquamates from the fingers and toes." Dorland's at 537.

[19] Compartment syndrome is "a condition in which increased tissue pressure in a confined anatomical space causes decreased blood flow leading to ischemia and dysfunction of contained myoneural elements, marked by pain, muscle weakness, sensory loss, and palpable tenseness in the involved compartment. Ischemia can lead to necrosis resulting in permanent impairment of function." Dorland's at 1825.

[20] Acidosis is "the accumulation of acid and hydrogen ions or depletion of the alkaline reserve (bicarbonate content) in the blood and body tissues, resulting in a decrease in pH." Dorland's at 16.

Complement[21] studies and IgM[22] were low the day before. Id. Neurologically, T.A. was sedated on Versed and Fentanyl. His Glasgow coma scores ranged from 3-6. Id.

On August 28, 2011, Dr. Heulitt wrote that T.A. was being managed for septic shock, acute renal failure, and possible meningococcal septicemia, but overnight T.A. developed demarcation in his lower extremities, bluing, and discoloration consistent with necrosis of the skin and possible loss of those extremities. Id. at 489. He was started on Synthroid the day before due to evidence of hypothyroidism. He was continued on mechanical ventilator support. T.A. had bilateral chest tubes in place for pleural effusions, with increased densities in the left lung. An echo cardiogram done the day before showed some left ventricular hypertrophy. He was on continuous venovenous hemodiafiltration ("CVVHD"). Id. T.A.'s glucose that morning was 229 and he was on an insulin infusion. Id. at 490. His wbc was 23,000. From an infectious disease standpoint, all of T.A.'s cultures were negative. Dr. Heulitt was stopping T.A.'s isolation that day. His Ehrlichia PCR, MRSA PCR, and staph pneumococcus PCR were all negative. On examination that morning, T.A. had marked changes in his lower extremities with blistering and further demarcation in his mid-calf area with the plan to get a formal burn consultation to look at his wounds. Overall, T.A. remained critically ill, requiring numerous medical interventions. Id.

Also on August 28, 2011, Burn Surgery was consulted due to discoloration of T.A.'s toes and feet which had progressed to blisters with extension up to his ankles. Id. at 523. It was determined that T.A. would need surgical intervention due to bilateral lower extremity limb ischemia secondary to vasoconstriction with open wounds. Id.

On August 29, 2011, Dr. Ronald Sanders wrote a critical care medicine note stating T.A. was being managed for four days for signs and symptoms consistent with septic shock, acute renal failure and rhabdomyolysis.[23] Id. at 492. The nurses wrote that he was moving around a little bit more and seemed to be responding to his loved ones. The infectious diseases specialist said T.A.'s cultures showed no growth so far and his PCRs had not revealed any etiology for his clinical picture. T.A. remained in acute renal failure. He remained critically ill and at high risk of death, but he was trending in the right direction and his current clinical progression was encouraging. Id.

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[21] The complement "pathway is initiated by binding of two antibody molecules to a multivalent antigen." Dorland's at 394 (schematic representation). Complement "is now used to refer to the entire functionally related system comprising at least 20 distinct serum proteins, their cellular receptors, and related regulatory proteins that is the effector not only of immune cytolysis but also of other biologic functions including anaphylaxis, phagocytosis, opsonization, and hemolysis." Id. at 393.

[22] IgM is "immunoglobulin M." Dorland's at 913. Immunoglobulin is "any of the structurally related glycoproteins that function as antibodies, divided into five classes (IgM, IgG, IgA, IgD, and IgE) on the basis of structure and biologic activity. … In addition to the effects produced solely by the binding of antigen by antibody, e.g., viral neutralization or the inability of some bacteria to invade mucosal surfaces when coated by antibody, certain classes of antibodies can trigger other processes when bound to antigen: IgM and IgG activate the classic complement pathway. . . ." Id. at 919.

[23] Rhabdomyolysis is "disintegration or dissolution of muscle, associated with excretion of myoglobin in the urine." Dorland's at 1637.

On September 1, 2011, Dr. Sanders wrote that T.A. had been successfully weaned off vasopressor support. Id. at 495. Due to elevated creatinine phosphokinase ("CPK") and the condition of T.A.'s lower extremities, it was highly likely that T.A. was going to require bilateral lower leg amputations. Id.

On September 2, 2011, Dr. Sanders wrote that T.A. was extubated the day before and was off all vasopressors. Id. at 497. He was moving air equally well in both lung fields. His lower extremities continued to be wrapped in sterile gauze. His lower extremities evidenced gangrenous changes superficially and the Burn Service was watching him very closely. His heart was normal. His abdomen was soft. He remained on broad spectrum antibiotics, including vancomycin, cefepime, and doxycycline. Pediatric Infectious Diseases recommended stopping the vancomycin that day. T.A. continued to make urine, but was not able to balance his input and output, and remained on CVVHD. Dr. Sanders would discuss with the Renal Service how much longer they would like to keep T.A. on CVVHD and when they planned to do intermittent hemodialysis. T.A. remained critically ill, but was moving in the right direction. His wbc remained elevated at 24,700. Id.

On September 3, 2011, Dr. M. Michele Moss wrote a critical care medicine note, diagnosing T.A. with respiratory insufficiency, sepsis, and renal failure. Id. at 499. T.A.'s heart rate increased to the 130s and 150s from the 90-100 range the day before. He was not febrile. His eyes were somewhat sunken and his input and output remained equal to somewhat negative. His lungs sounded clear. His lower extremities remained ischemic with wraps. His white count was a little bit higher every day and some of that might be a leukemoid reaction,[24] although most of the cells were actually lymphocytes. Id.

On September 4, 2011, Dr. Adnan T. Bhutta wrote a critical care medicine note, diagnosing T.A. with septic shock, acute renal failure requiring CVVHD, and myositis[25] in the lower extremity with associated skin ischemia. Id. at 501. The Burn Team said T.A.'s legs have improved markedly. He was scheduled to go to the operating room for grafting. Id.

On September 5, 2011, Dr. Moss wrote that T.A. continued to show improvement. Id. at 503. T.A. was awake enough to ask for lemonade and was clearly thirsty. He was less shaky, but remained on low-dose morphine infusion for pain. He was to go to the operating room the next day for debridement[26] of his lower extremities. T.A. was tolerating full feeds and was stooling. His liver function tests were improving. He had a fever that morning. Id.

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[24] A leukemoid reaction is "a peripheral blood picture resembling that of leukemia or indistinguishable from it on the basis of morphologic appearance alone, with leukocytosis of varying degrees and increased numbers of immature cells in circulation. It may be seen with infections such as tuberculosis, brucellosis, toxoplasmosis, staphylococcal infections, and streptococcal infections; with inflammatory disorders such as glomerulonephritis, rheumatoid arthritis, liver failure, and diabetic acidosis; with tumors and granulomatous infiltration of bone marrow; and with intoxications such as eclampsia, severe burns, and mercury poisoning." Dorland's at 1600.

[25] Myositis is "inflammation of a voluntary muscle. . . ." Dorland's at 1225.

[26] Debridement is "the removal of foreign material and devitalized or contaminated tissue from or adjacent to a traumatic or infected lesion until surrounding healthy tissue is exposed." Dorland's at 473.

On September 6, 2011, Dr. Anjay Khandelwal performed bilateral guillotine below-knee amputations[27] on T.A. because of bilateral lower extremity limb ischemia secondary to vasoconstriction with open wounds. Id. at 538. He had necrotic muscles of all three compartments in the lower extremities. Id. He also had metabolic acidosis and needed to remain intubated. Id. T.A. presented to Arkansas Children's Hospital with evidence of sepsis. Id. In order to perform perfusion and a blood pressure, he was started on vasopressors and subsequently developed renal failure. Id. at 538-39. He developed significant vasoconstriction and his vasculature clamped down, resulting in ischemia to his bilateral lower extremities. Id. at 539. When Surgery was consulted, T.A. had evidence of limb ischemia with some dry gangrene of his toes and ischemic discoloration with blistering of his lower extremities. It was not evident at the time that he had compartment syndrome. Id. On examination of the lower extremities, Dr. Khandelwal noted T.A. had persistent gangrene of his toes. The dry gangrene and necrosis of his feet had progressed and he had significantly dark, ischemic-dried gangrenous areas present on his lower extremities, extending about ¾ proximally up his bilateral calves. Dr. Khandelwal examined all three muscular compartments within the calf by performing a fasciotomy.[28] There was minimal bulging of the muscle upon releasing the fascia. However, the muscle underneath was dark and nonperfused. The muscle did not bleed and was not stimulated when Dr. Khandelwal used a Bovie electrocautery. The muscle did not have just an ischemic appearance, but almost a frankly necrotic appearance. There was no wet gangrene of infection. Upon consultation with Dr. Sam Smith from Pediatric Surgery, they agreed on the need to amputate. Id. Bilateral below-knee amputations were performed in hopes of salvaging the knees. Id. at 540. The tibia and fibula on both sides were transected using the saw. The doctors preserved as much of the viable skin as they could. Hemostasis[29] was secured. Amputation sites were left as guillotine amputations. Toward the end, T.A. became a little hypotensive with a bump up in his acidosis. He was transferred back to pediatric intensive care unit intubated. Id.

On September 7, 2011, Dr. Stephen M. Schexnayder wrote a critical care medicine note. Id. at 506. T.A. had hyperkalemia[30] after returning from the operating room from his bilateral amputation the day before. CVVHD was started back overnight. He required some volume resuscitation. He has had some ongoing hypotension. He was febrile overnight and vancomycin and meropenem[31] were begun. They would keep T.A. intubated and mechanically ventilated. Dr. Schexnayder diagnosed T.A. with hypotension and respiratory failure. Id.

On September 8, 2011, Dr. Schexnayder wrote that T.A. returned to the operating room

[27] Guillotine amputation means "rapid amputation of a limb by a circular sweep of the knife and cut of the saw, the entire cross-section being left open for dressing; done when primary closure of the stump is contraindicated, owing to the possibility of recurrent or developing infection." Dorland's at 68.

[28] Fasciotomy is a "surgical incision or transection of fascia, often performed to release pressure in compartment syndrome." Dorland's at 685. Fascia is a sheet or band of fibrous tissue such as lies deep to the skin or forms an investment for muscles and various other organs of the body." Id. at 679.

[29] Hemostasis means "arrest of bleeding." Dorland's at 843.

[30] Hyperkalemia is "abnormally high potassium concentration in the blood, most often due to defective renal excretion." Dorland's at 890.

[31] Meropenem is "a broad-spectrum antibiotic of the carbapenem group, similar to imipenem in structure and activity and used in the treatment of intra-abdominal infections and bacterial meningitis. . . ." Dorland's at 1137.

that day for debridement of his extremities and to assess their viability. Id. at 507. His diagnosis was sepsis with organ dysfunction. Id. Later that same day, Dr. Schexnayder wrote that T.A. might have to be converted to bilateral above-knee amputations. Id. at 509. He was going to request Immunology to assess T.A. because of the severe nature of illness with a negative culture although he received IV antibiotics and this would be consistent with meningococcal infection. Id.

On September 12, 2011, Dr. Khandelwal wrote a further operative note for bilateral lower extremity limb ischemia secondary to sepsis and suspected *Neisseria*[32] meningitis, and status post-bilateral guillotine below-the-knee amputations. Id. at 541. He performed bilateral above-knee amputations. Id. T.A. had a complication of hypoxemia[33] requiring persistent intubation. Id. On examination of T.A.'s stumps, Dr. Khandelwal found that the muscle was still persistently necrotic over both lower extremities, thereby necessitating above-knee amputations. Id. at 542. A fish-mouth incision was marked on both lower extremities above the knee with attempts to preserve as much of the skin flap as possible as well as to preserve as much length in the femur[34] as possible. On the right-hand side, Dr. Khandelwal made a skin incision with the scalpel and carried it down through fat and subcutaneous tissue. For further dissection, he used Bovie electrocautery. Dissection carried down through the muscular compartments. Once he reached T.A.'s femur, Dr. Khandelwal used a periosteal elevator[35] to strip the periosteum from the femur. At the beginning of the condyle,[36] Dr. Khandelwal transected the femur with the bone saw. Id. On the left lower extremity, after making a similar fish-mouth incision, and incising skin and fat, Dr. Khandelwal noted the quadriceps tendon was ischemic although some of T.A.'s larger vessels appeared to have flow. The muscle appeared slightly ischemic but not necrotic. It was very weakly contractile with the Bovie electrocautery. But some of the musculature was not at all contractile and therefore Dr. Khandelwal excised this musculature sharply with the Bovie electrocautery. Id. He transected the bone with the saw at a similar length and in a similar fashion as on the right-hand side. Id. at 543. In light of the slightly ischemic nature of the muscles, Dr. Khandelwal decided to close the wound with a wound VAC to increase circulation and bring T.A. back to the operating room over the next several weeks to perform an ultimate closure. Id. Dr. Khandelwal informed T.A.'s family that the length of the

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[32] *Neisseria* is "a genus of bacteria of the family Neisseriaceae, consisting of gram-negative, oxidase-positive cocci characteristically coffee bean-shaped and paired. The organisms are aerobic or facultatively anaerobic and are part of the normal flora of the oropharynx, nasopharynx, and genitourinary tract. The genus includes the gonococcus, the several meningococcus types, pigmented forms occasionally associated with meningitis, and a number of saprophytic or parasitic but nonpathogenic species." Dorland's at 1237. *Neisseria meningitidis* is "a prominent cause of meningitis and the specific etiologic agent of meningococcal meningitis; it can also cause meningococcal pneumonia, a type of bacterial pneumonia . . . ." Id. Meningitis is "inflammation of the meninges, usually by either a bacterium . . . or a virus . . . ." Id. at 1132. Meninges are "the three membranes that envelop the brain and spinal cord: the dura mater, pia mater, and arachnoid." Id.

[33] Hypoxemia is "deficient oxygenation of the blood." Dorland's at 908.

[34] Femur is "the bone that extends from the pelvis to the knee, being the longest and largest bone in the body . . . [;] distally, the femur, along with the patella and tibia, forms the knee joint." Dorland's at 688.

[35] An elevator is "an instrument for lifting tissues . . . ." Dorland's at 604. A periosteum elevator is "a flat steel bar for separating the attachments of the periosteum to bone." Id. Periosteum is "a specialized connective tissue covering all bones of the body, and possessing bone-forming potentialities. . . ." Id. at 1417.

[36] Condyle or condylus is "a rounded projection on a bone . . . ." Dorland's at 402.

left leg might end up shorter than the right leg. Id.

Also on September 12, 2011, Dr. Parthak Prodhan wrote a critical care medicine note, diagnosing T.A. with acute respiratory failure; septic shock meningococcemia, query; acute kidney injury; and above-knee amputation secondary to ischemia of the lower extremities. Id. at 519. T.A. was currently not on any antibiotics. He was on steroids for relative adrenal insufficiency. Id.

On September 13, 2011, Dr. Prodhan wrote that T.A. was slightly puffy and had pain issues. Id. at 521. He was on fentanyl. Id.

On September 20, 2011, T.A.'s bedside nurse called social worker Esther Pipkin to say T.A.'s bandage fell off while he was in the play room and he became upset. Id. at 1827. T.A. was now more awake and alert. The social worker and T.A.'s family had been talking to T.A. about his legs, but it was unclear if he understood part of his legs was removed. T.A. had looked at the legs but not made any comments. When Ms. Pipkin entered the playroom, T.A.'s mother was in bed with T.A. reading a book that Ms. Pipkin provided regarding a horse who lost a leg and had a prosthetic placed. Id. T.A. turned toward his mother, crying, "Put my legs back on." Ms. Pipkin started talking to T.A. about his legs when T.A. stated, "I want my white legs on." Id. T.A.'s father arrived in the playroom and stated T.A. wanted the bandage put back on his leg. The father explained the Burn Team was coming up to put a new bandage on T.A.'s leg. T.A. continued to cry, stating he wanted the white bandage. Ms. Pipkin went to the nurse to see if it was okay to put a temporary dressing on the leg until the Burn Team arrived. The nurse was willing. Ms. Pipkin explained to T.A. that the nurse was in the playroom to put the "white leg" back on and T.A. immediately calmed down. T.A.'s father assisted the nurse in putting the bandage on and T.A. calmed down and went to sleep. Ms. Pipkin explained to the parents the need for T.A. to be involved in medical play and to do express activities to assist with the loss. T.A.'s father asked about the movie "How to Train Your Dragon" which involves the loss of a leg and the use of a prosthetic. Ms. Pipkin encouraged T.A.'s parents to get the movie and see how T.A. responds. Ms. Pipkin felt T.A.'s reaction to seeing his leg with an incision and no bandage was frightening to him. She was still unsure if T.A. understood he lost part of his legs, but once the bandage was off, he could see it and she felt it scared him. She felt T.A.'s age made understanding his loss difficult due to children that age being magical thinkers. Her plan was to assist with grief and loss issues. Id.

On September 22, 2011, Amelia H. Randag, a child life specialist, wrote that she met with T.A. and his grandmother to begin a play session. Id. at 1830. T.A. had limited use of his hands; therefore, Ms. Randag allowed T.A. to choose the colors to decorate the teaching doll, and followed T.A.'s instructions. T.A. chose his grandmother to play the role of the doctor and Ms. Randag to play the role of the nurse. Id. T.A. was more avoidant when the medical play session began, not answering Ms. Randag's questions throughout the play session, but did answer her questions when Ms. Randag offered choices. The grandmother played through T.A.'s admission to the prior hospital, air evacuation via Angel One, various tests and medications that were tried to "get rid of" T.A.'s virus, and eventually the surgery when T.A.'s

legs were amputated. Ms. Randag explained that the medicine was not helping and the only way to make T.A. "well" was to get rid of the part of his legs that was making him sick. She explained that T.A. did nothing wrong to cause the amputation. T.A. turned his head away during this portion of the play session. The grandmother took off her doctor's hat and mask, and Ms. Randag interpreted this as a cue to end the session. T.A. agreed to continue the play at a later time. Ms. Randag encouraged T.A. to continue "doctoring" on the teaching doll when he felt like it. Ms. Randag returned later that evening to follow up, but T.A. was being bathed. Ms. Randage explained to the grandmother the goals for future play sessions: (1) to ensure T.A. knows the amputation is not a punishment, and (2) to ensure T.A. knows that his family will still love him and take care of him. These are common fears for this age. Id.

On September 26, 2011, Dr. Khandelwal wrote an additional operative note to revise the right above-knee amputation with closure. Id. at 545. The muscle on top of the stump appeared viable, but there was some fat that, although slightly ischemic, appeared to be improving over the past several dressing changes. Id. at 545-46. He excised sharply using a scalpel some residual tissue. Id. at 546. Dr. Khandelwal released muscle from the periosteum using a periosteal elevator, and freeing the femur. He then resected a portion of the femur using a bone saw and shaped the femur to prevent any sharp edges. Id.

On September 28, 2011, occupational therapist Frank H. Bregy met with T.A. to help with hand splints, but T.A. continued to be agitated, refusing activity. Id. at 1832. T.A. was verbalizing his requests and would state "yes" when asked if he would like to do a specific activity, but when presented, he would refuse and begin to yell and become more upset. Id. Later, on the same day, physical therapist Suzanne L. Shepard noted T.A. continued to be agitated and to refuse to participate in therapist-directed activities. Id. at 1833.

On October 3, 2011, Ms. Shepard noted that T.A. was much more alert and participatory. Id. at 1836. He could sit independently for 15 seconds at a time without upper extremity support before requiring assistance. He did not complain of pain and was noted to be laughing or smiling periodically. Id.

On October 4, 2011, Ms. Shepard noted T.A. could sit without upper extremity support for 25-30 seconds. He demonstrated good weight bearing through his bilateral upper extremities while sitting as well as transfer weight between his arms. He did not complain of pain and was noted to be laughing or smiling periodically. Id. at 1837.

On October 5, 2011, social worker Marybeth D. Evans noted she met with T.A.'s mother and grandmother to assess their needs and provide support for discharge issues. Id. at 1838. T.A.'s mother said they will go home with a borrowed wheelchair. She expected they would get a fitting for prostheses in a couple of weeks. Shriners, to whom they contributed in the past, invited them to have T.A. assessed for services there. T.A. was looking happy "tooling down the hallway in his little wheelchair." Id.

On October 5, 2011, T.A. was discharged from the hospital. Id. at 523. Dr. Anjay

Khandelwal attended and APN Jayna C. Harper wrote the diagnosis was sepsis with bilateral lower extremity necrosis resulting in bilateral above-knee amputation. Id. at 525, 527. Infectious Diseases' working differential diagnosis was tick-borne illness vs. meningococcemia and DIC. Id. at 524. T.A. developed diffuse petechiae throughout early hospitalization. He did not have purpura[37] or desquamation.[38] Id. His feet gradually became darker likely secondary to vasoconstriction vs. septic emboli. Doctors determined T.A. needed surgical intervention due to bilateral lower extremity limb ischemia secondary to vasoconstriction with open wounds. Id.

On October 7, 2011, T.A. returned to Arkansas Children's Hospital with abdominal pain, dehydration, drug withdrawal, and drug dependence. Id. at 987. He was discharged on October 12, 2011. Id.

On October 12, 2011, T.A. saw Dr. Jonathan Swenson and Dr. Esther H. Tomkins for a physical medicine and rehabilitation consultation. Id. at 954. Dr. Swenson wrote that T.A. was hospitalized due to septic shock likely due to meningococcemia. Id. T.A. was recently discharged from Arkansas Children's Hospital but readmitted shortly thereafter due to several episodes of emesis and abdominal pain. He was diagnosed with opioid withdrawal and was restarted on a slow taper of methadone. He had suspected spasticity in his left upper extremity which might need Botox. Id. T.A. complained occasionally that his foot and ankle hurt, consistent with phantom limb pain. Id. at 965. He had decreased functional use of his left hand and wrist. On physical examination, he had moderate finger flexion contracture in his left hand with atrophy of the intrinsic hand muscles on the left and some thenar[39] atrophy. The hand had the appearance of a claw hand, but included the second and third digits. He had a mild amount of wrist drop. The right hand was minimally affected in the same pattern distribution as the left hand, but he could use the right hand. This could have been due to compressive neuropathy due to his severe edema while in ICU or to positioning in bed. It appeared the compressive neuropathy affected the ulnar and median nerves to the greatest degree and, to some degree, the radial nerve. Id. Dr. Swenson explained to T.A.'s family that this was not likely due to a brain problem but most likely related to focal damage of the peripheral nerves in T.A.'s forearms. Id. Dr. Swenson recommended occupational therapy and physical therapy, stating Botox was not indicated as T.A. did not have true spasticity. Id. at 976.

On October 18, 2011, T.A. returned to Dr. Allen after his prolonged hospitalization at Arkansas Children's Hospital to which he was transferred two months earlier with a diagnosis of probable sepsis and hypovolemia.[40] Med. recs. Ex. 3, at 17.

On October 24, 2011, T.A. saw Dr. Allen. Id. at 19. Dr. Allen notes that T.A.'s legs

[37] Purpura is "any of a group of conditions characterized by ecchymosis or other small hemorrhages in the skin, mucous membranes, or serosal surfaces; causes include blood disorders, vascular abnormalities, and trauma." Dorland's at 1557.

[38] Desquamation is "the shedding (exfoliation) of epithelial elements, chiefly of the skin, in scales or sheets." Dorland's at 501.

[39] Thenar is "the mound on the palm at the base of the thumb." Dorland's at 1909.

[40] Hypovolemia is "abnormally decreased volume of circulating blood in the body; the most common cause is hemorrhage." Dorland's at 908.

were amputated because of ischemia[41] with possible sepsis. T.A. also had some nerve damage to his left hand, which was fisted. He had some behavioral problems over the weekend. He threw some paint and threw a cake; when he got upset, he became very aggressive toward anyone near him. T.A. still did not make eye contact or smile. Id. T.A. had above-the-knee amputations bilaterally. He had depression and behavioral problems. He was on amitriptyline, but Dr. Allen did not know if that was effective. T.A. was tapering his methadone. Dr. Allen wrote a prescription for Prozac. Id.

On November 14, 2011, T.A. saw Dr. Amy M. Scurlock, an allergist/immunologist, at the Arkansas Children's Hospital Allergy/Immunology Clinic. Med. recs. Ex. 7, at 77. Dr. Scurlock had previously seen T.A. when he was hospitalized from August through early October 2011. Id. T.A.'s mother gave a history that about one week prior to his hospitalization, T.A.'s feet hurt and he was more lethargic and irritable. Id. at 78. T.A. had received MMR vaccine about two weeks prior to his hospitalization. Dr. Scurlock wrote, "With our current data that we have now, I cannot clearly implicate or not implicate the vaccine." Id. Dr. Scurlock states, "Unfortunately we were unable to clearly identify an infectious etiology. It is a presumed infectious etiology but he did receive some antibiotics prior so we were unable to culture anything." Id. T.A.'s mother said that, in comparison with T.A.'s brothers, he seemed to pick up infections more easily. Id. On lab testing, T.A.'s natural killer cell count was elevated. Id. at 79. Dr. Scurlock wrote that T.A. never developed the true purpura, although he did have petechiae. Id. T.A. also had a history of lymphopenia[42] while hospitalized which continued to improve, and he had an abnormal immune test. Id.

On December 2, 2011, T.A. saw Dr. Perry Schoenecker at Shriners Hospitals for Children for evaluation for prosthetic care. Med. recs. Ex. 14, at 1. Dr. Shoenecker writes that a physician told T.A.'s mother that T.A. could have had an immunologic response to vaccination vs. possible meningococcemia, but it would never be able to be proven. Id. Dr. Schoenecker comments that T.A. has had some difficulties with sleeping because he went to sleep when he had his amputations and when he woke up, he had no legs. He has become very apprehensive about sleep. He mostly scoots around. Id.

On February 6, 2012, T.A. saw Dr. Barbara Saunders for a habilitation consultation. Med. recs. Ex. 7, at 44. She described him as status post-bilateral transfemoral amputation secondary to infection, likely meningococcemia. Id. During his hospitalization, he developed a compressive neuropathy with radial nerve injuries bilaterally. The left hand seems to be more affected than the right. He kept his left hand in a loose fist but easily opened it when reminded. T.A. tended to crawl on the heel of his hand and his wrist to push his wheelchair. He had difficulty with balance during transfers because of keeping his hand held in this position. Id. T.A. was an active, well-appearing little boy. He showed off his break dancing skills during the physical examination. Id.

[41] Ischemia is "deficiency of blood in a part, usually due to a functional constriction or actual destruction of a blood vessel." Dorland's at 961.

[42] Lymphopenia is lymphocytopenia which is "reduction in the number of lymphocytes in the blood. . . ." Dorland's at 1085.

On May 14, 2012, T.A. saw Dr. Scurlock again for an evaluation. Med. recs. Ex. 7, at 27. Her diagnosis was abnormal immune disorder, lymphopenia. Id. at 21. As an infant, T.A. had a staphylococcal infection at age 5-6 months. Id. at 28. T.A.'s mother said he had been sicker than other children. Id. On lab testing that day, T.A.'s AST was 58, whereas the normal range is 15-50. Id. at 28-29. His ALT was 44, whereas the normal range is 10-25. Id. at 29. Dr. Scurlock sent panels to Cincinnati, including an ALPS[43] panel, because one of T.A.'s brothers has an increased double negative T cell count and he did have "this response" (the brother tested positive to the ALPS panel). Id. Dr. Scurlock's impression was that T.A. has a history of abnormal immune studies with lymphopenia (reduction in the number of lymphocytes in the blood) primarily. Id. at 29. Her differential diagnoses for T.A. included: (1) infection, status post-vasopressors,[44] and (2) infection and meningococcemia. She found it interesting, however, that he never developed a true purpura, although he did have some petechiae with meningococcemia.[45] Id.

Also on May 14, 2012, Dr. Scurlock had Arkansas Children's Hospital do laboratory tests on T.A. Id. at 3. In special immunology studies, T.A. had a high percentage of gamma delta cells, i.e., 10, when the normal range is 1-5. Id. at 6. He had a low percentage of CD4 T helper cells,[46] i.e., 31, when the normal range is 35-51. Id. T.A. had a low percentage of alpha beta T cells, i.e., 90, when the normal range is 95-97. Id. at 7. He had a high percentage of CD45RA T SUPRS, i.e., 92, when the normal range is 60-90, but a low percentage of CD45RO T SUPRS, i.e., 8, when the normal range is 10-40. Id. Dr. Terry Harville, Medical Director of the Special Immunology Laboratory, concluded T.A. exhibited an essentially normal immunophenotype. He could not identify the cause of T.A.'s recurrent infections by specific immunodeficiency. T.A. had a low normal-for-age CD4 T lymphocyte count. Id. at 14. T.A. was given an ALPS test for which he tested normal. Id. at 17. He was given a cytotoxic T-lymphocytes ("CTL")[47] function test and the result was decreased CTL function. Id. at18.

On July 25, 2012, T.A. returned to Dr. Schoenecker at Shriners Hospitals for Children because he may have gotten a splinter in his right stump while crawling through the grass the day before without any protection or prosthetic on. Med. recs. Ex. 14, at 4. His right stump was warm, red, and swollen. Id. The doctor found a single puncture wound in the middle of the erythema. Id. at 5. The doctor admitted T.A. to the hospital and placed him on IV antibiotics.

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[43] ALPS is "autoimmune lymphoproliferative syndrome." Dorland's at 54. Autoimmune lymphoproliferative syndrome is "a hereditary disorder of lymphocyte apoptosis that results in the accumulation of large numbers of mature lymphocytes in the lymph nodes and spleen, appearing during childhood and characterized by massive lymphadenopathy, splenomegaly, and autoimmune hemolytic anemia and other cytopenias." Dorland's at 1822.

[44] A vasopressor is a "1. stimulating contraction of the muscular tissue of the capillaries and arteries. 2. an agent that stimulates contraction of the muscular tissue of the capillaries and arteries." Dorland's at 2027.

[45] Meningococcemia is "invasion of the bloodstream by meningococci." Dorland's at 1133.

[46] Helper T cells are "differentiated T lymphocytes whose cooperation (help) is required for the production of antibody against most (T-dependent) antigens. . . . [H]uman helpers cells [are marked] by the CD4 antigen." Dorland's at 318.

[47] Cytotoxic T lymphocytes are "differentiated T lymphocytes that can recognize and lyse target cells bearing specific antigens recognized by their antigen receptors. . . . These lymphocytes are important in . . . killing of . . . virus-infected host cells. . . . Called also *killer* or *killer T cells.*" Dorland's at 1084.

Id. On July 26, 2012, Dr. Schoenecker did irrigation and debridement on T.A.'s right stump. Id. at 8. A large pocket of fluid was seen mostly straw-colored with a few purulent areas. Id. at 9. T.A. was discharged on July 27, 2012 on oral antibiotics. Id. at 11.

On October 11, 2016, T.A. had a test for *Neisseria meningitidis* Ag. Med. recs. Ex. 54. The test result was negative.[48] Id. at 1.

On February 9, 2018, petitioners filed a HIPPA amendment to Arkansas Children's Hospital discharge diagnosis. Ex. 56. Petitioners requested T.A.'s medical records be revised. Id. at 3. On August 30, 2017, petitioners met with Chief Medical Officer Dr. Jayant Deshpande, infectious diseases specialist Dr. Jose Romero, and two risk management liaisons to discuss their concerns about T.A.'s medical records and what they wanted amended. Id. Subsequently, Dr. Deshpande wrote an addendum to T.A.'s chart, stating he would modify T.A.'s final discharge diagnosis to read: "(1) sepsis syndrome with bilateral lower extremity necrosis; (2) bilateral above-knee amputations." Id. at 5.

On May 29, 2018, petitioners filed e-mail correspondence between the surgeon Dr. Anjay Khandelwal and themselves. Ex. 57. Dr. Khandelwal writes that his "strong belief" is that the necrosis of T.A.'s skin and muscle was likely from the pressors and his overall illness. Id. at 3. "They are not typical for purpura fulminans[49] as seen with meningitis – in fact in my initial consult, I remarked that I did not think the diagnosis was purpura fulminans." Id.

Medical Expert Reports

Petitioners filed a statement from Dr. L. Barry Allen, T.A.'s treating pediatrician, in which he says that, on August 11, 2011, T.A. came to his office for his three-year-old well child examination. Ex. 18, at 1. T.A. was doing well and did not have any problems. T.A. received MMR vaccine on that date. Thirteen days later, T.A. returned to Dr. Allen's office with a fever of 102 degrees and a macular and petechial rash. His platelets were low and his white blood cell count was normal. He gave T.A. Rocephin and requested T.A. return the next day. On August 25, 2011, T.A. returned and was quite lethargic. His white blood cell count was elevated and his platelets lower than the day previous. Dr. Allen thought he had either an infection or an adverse reaction to MMR vaccine since the timing of the vaccination two weeks before was a red flag for causation. Id. Numerous tests failed to identify a bacterial or viral etiology. Id. at 2. Dr. Allen concludes that MMR vaccine probably caused T.A.'s symptoms, not only because the timing

[48] The cover page to this filing states it is antibody testing, but the test result refers only to *N. meningitidis* Ag. Med. recs. Ex. 54, at 1. "Ag" means "antigen." Dorland's at 37. The undersigned has no idea if more than five years after T.A. became ill, if he had been exposed to *Neisseria meningitidis*, the antigen would still be present in his body. Moreover, the undersigned has no idea if the absence of *Neisseria meningitidis* antigen equals negative antibody to it. Petitioners never filed a doctor's report to explain the significance of Exhibit 54. Therefore, the undersigned does not base any finding upon this test result.

[49] Purpura fulminans is "a form of nonthrombocytopenic purpura seen mainly in children, usually following an infectious disease such as scarlet fever or varicella; characteristics include fever, shock, anemia, and sudden and rapidly spreading symmetrical skin hemorrhages of the lower limbs, often with extensive intravascular thromboses and gangrene." Dorland's at 1557.

was perfect, but also because an adverse reaction to MMR vaccine would cause an increase in white blood cells and neutrophils and a reduction in leukocytes. Id. Dr. Allen attributes T.A.'s ultimate bilateral amputations and permanent neurological deficits to his adverse reaction to MMR vaccination. Id.

Petitioners filed an initial opinion of their expert pediatric neurologist Dr. David J. Siegler, dated October 4, 2012. Ex. 10. He states that T.A. had a vaccine-induced encephalitis, indicating a vaccine-related adverse event. Id. at 1. T.A.'s depressed level of consciousness with fever and rash developing 12 days after MMR vaccination supports causation. Id. At the time he wrote his expert report, Dr. Siegler maintained a clinical practice as well as acted as Clinical Assistant Professor at Oklahoma University State College of Osteopathic Medicine, Department of Pediatrics. Ex. 11, at 1.

Respondent filed a report of his expert pediatric neurologist Dr. Lawrence W. Brown, dated July 24, 2013. Ex. A. Dr. Brown states he has had almost 35 years of experience managing critically ill children with neurological disease. Id. at 1. T.A. presented with fatigue and low-grade fever followed quickly by spiking fever, petechial rash, vomiting, diarrhea, and rapid decline with multisystem involvement, i.e., septic shock. He received MMR vaccine about 10 days before the onset of illness. Id. In the hospital, T.A. had a markedly abnormal complete blood count with dramatic shift to the left, thrombocytopenia (platelets 23,000), and signs of coagulopathy. Id. at 2. Over his first few days of PICU, T.A. was comatose, but improved within days. T.A. did not have signs of meningitis or focal neurologic deficits. Id. T.A.'s doctors never considered T.A. had meningoencephalitis by obtaining a lumbar puncture or T.A.'s central nervous system to be a primary target of his illness by doing an EEG or MRI. Id. The doctors did an extensive and comprehensive infectious diseases search considering everything from meningococcemia as the most likely cause to Ehrlichia, rickettsia, MRSA, pneumococcus, and tularemia. Id.

Dr. Brown's opinion is that the combination of fever, vomiting, petechial rash with thrombocytopenia, hypotension despite adequate fluid resuscitation, oliguria,[50] hypoxia, and coma is most consistent with septic shock. He states, "It is unfortunate that no definitive organism was found. . . ." Id. Dr. Brown states that T.A. did not have acute measles encephalitis, which typically presents with headache, irritability, somnolence, seizures and coma with occasional ataxia, chorea or focal deficits. It does not start with diarrhea, vomiting, petechial rash, and shock. Cerebral spinal fluid ("CSF") pleocytosis is the rule. The only symptom that T.A. had that would be consistent with MMR encephalitis was altered awareness. Id. The attending physicians never considered T.A. had encephalitis. Id. at 3. Only in December 2011 when T.A. was in Shriner's Hospital being evaluated for prostheses was immunization first implicated. Dr. Perry Schoenecker wrote that T.A.'s parents were told T.A.'s condition could have been an immunologic response to MMR or meningococcemia, but the etiology could not be proven. Id. Dr. Brown concludes by saying that no specific etiology was found for T.A.'s illness. Id. He notes that septic shock is a syndrome that many viruses or bacteria can cause, but vaccinations are not a "known etiology." Id.

[50] Oliguria is "diminished urine production and excretion as compared with fluid intake. . . ." Dorland's at 1318.

Dr. Brown's CV shows extensive training, clinical experience, academic appointments, numerous awards, honors, memberships in honorary and scientific societies, and extensive publications. Ex. A, Tab 1.

Respondent filed a report of his pediatric infectious diseases expert Dr. Jerome O. Klein, dated April 25, 2013. Ex. B. Dr. Klein writes T.A. had septic shock, a multisystem disease associated with acute respiratory failure, acute renal failure, DIC, and vascular insufficiency of the lower extremities resulting in ischemia followed by extensive tissue damage necessitating above the knee amputations. Id. at 3. Dr. Klein states septic shock is usually due to extensive bacterial infection such as meningococcemia or pneumococcal or streptococcal bacteremia. He says it is likely that the intramuscular injection of ceftriaxone on August 24, 2011 had bactericidal concentrations in the blood sufficient to suppress growth of the causative organisms. It is also possible that a tick-borne disease such as Rocky Mountain spotted fever caused T.A.'s septic shock. Id. Dr. Klein denies that T.A. had encephalopathy. Dr. Klein states he knows of no similar case in which MMR caused septic shock. Id. Even though T.A. received MMR vaccine eleven days prior to onset of his septic shock, "there are no data that would indicate MMR could be a causative factor in developing of septic shock and the sequelae of tissue damage requiring amputations." Id. at 4. He denies that T.A. had SIRS from MMR vaccine because SIRS occurs within minutes to hours after administration of the provocative agent. Dr. Klein states, "It is biologically implausible that administration of MMR on August 11 would be responsible for a cytokine storm 11 days after vaccination." Id. Dr. Klein says thrombocytopenia is one of many features of organ dysfunction associated with sepsis syndrome, but it is the result, not the cause, of the coagulopathy that sepsis causes. The thrombocytopenia was responsible for the ischemia of T.A.'s tissues leading to lower limb amputations. Pathogens responsible for sepsis syndrome include pneumococcus, meningococcus, and streptococcus which the antibiotic T.A. receive on August 24th, i.e., ceftriaxone, inhibited. Therefore, Dr. Klein states, when doctors cultured T.A.s blood, he still had a concentration of ceftriaxone in his blood sufficient to suppress growth of these organisms, leading to a negative result. Id.

Dr. Klein's CV shows extensive training, clinical experience, academic appointments, numerous awards, honors, memberships in honorary and scientific societies, and extensive publications. Ex. B, Tab 1. Respondent later filed Dr. Klein's updated CV as Exhibit J.

Respondent filed a supplemental expert report from Dr. Brown, pediatric neurologist, dated February 11, 2014, stating that since an infectious septic shock unrelated to MMR vaccine caused T.A.'s altered mental status, T.A.'s medical complications do not qualify as a Table encephalopathy. Ex. C, at 1. Dr. Brown states there is no doubt that T.A. had encephalopathy within the time frame after MMR immunization, but his encephalopathy was just one component of septic shock. Id. at 3. Dr. Brown agreed that the live attenuated virus in measles vaccine can cause encephalopathy. Id. T.A.'s petechiae were completely different from the morbilliform[51] rash seen in a measles reaction. Id.

[51] Morbilliform means "like measles; resembling the eruption of measles." Dorland's at 1180.

Respondent filed a supplemental expert report from Dr. Klein, infectious diseases specialist, dated February 11, 2014. Ex. D. Dr. Klein states the rash that T.A. had was not red, blotchy, beginning on his head and progressing to his feet within three days. Id. at 5. T.A. had a petechial rash, which is small hemorrhages in the skin. T.A. did not have a rasping cough, conjunctivitis, or Koplik spots[52] characteristic of measles. Id. Dr. Klein concludes T.A. did not have vaccine-induced measles. Id. Dr. Klein notes that T.A. had thrombocytopenia which his sepsis caused. The thrombocytopenia did not cause the sepsis. Id. Dr. Klein states that only blood-borne bacteria can cause sepsis. Id. at 6. The reason cultures of T.A.'s blood were negative is because he had received the antibiotic ceftriaxone. Id.

Petitioners filed an expert report from Dr. Alan S. Levin, an immunologist, dated May 6, 2014. Ex. 19. He writes that he has treated over 100 patients with septic shock, systemic inflammation, organ dysfunction, and organ failure. Id. at 1. His opinion is that T.A. did not have septic shock but SIRS. Id. at 2. He agrees with Dr. Klein that T.A.'s receipt of ceftriaxone on August 24, 2011 would have suppressed growth of a bacterium initially, but given the protracted course and worsening of T.A.'s SIRS, subsequent histopathology specimens and cultures would have indicated a bacterial etiology if there were one. Thus he states T.A. did not likely have bacteria-induced septic shock. Dr. Levin's opinion is that MMR caused T.A.'s encephalopathy and SIRS. Id. He explains that inflammation[53] is a body's response to a nonspecific insult that can have various causes, including vaccines, since vaccination provokes an immune response and cytokine release. Id. at 1. Cytokine release overwhelmingly leads to activation of the endothelial system and loss of circulatory integrity, resulting in end organ dysfunction. Id. The time period between T.A.'s August 11, 2011 MMR vaccination and his onset of symptoms on or before August 24, 2011 is appropriate for the occurrence of an immune response. Id.

Petitioners filed a supplemental expert report from Dr. Siegler, pediatric neurologist, dated May 9, 2014. Ex. 22. Dr. Siegler states that T.A.'s history suggests non-infectious, autoimmune-mediated shock syndrome which MMR vaccine triggered. Id. at 2. He developed fever, macular rash, and thrombocytopenia 13 days after MMR vaccination, followed the next day by diarrhea and encephalopathy. Id. Dr. Siegler said strong consideration should be given to systemic inflammatory response syndrome ("SIRS"), a clinical syndrome describing shock and multiple organ dysfunction responses to a nonspecific insult due to either infectious (bacterial, viral, fungal, parasitic) or non-infectious (trauma, dehydration, drug reactions, autoimmune disorders) causes. He writes MMR was the known autoimmune trigger of T.A.'s SIRS 12-14 days post-vaccination. Id. There was no diagnostic evidence for bacterial etiology.

[52] Koplik sports are "small, irregular, bright red spots on the buccal and lingual mucosa, with a minute bluish white speck in the center of each; seen in the prodromal state of measles." Dorland's at 1756.

[53] Inflammation is "a localized protective response elicited by injury or destruction of tissues, which serves to destroy, dilute, or wall off (sequester) both the injurious agent and the injured tissue. It is characterized in the acute form by the classical signs of pain (dolor), heat (calor), redness (rubor), swelling (tumor), and loss of function (functio laesa). Histologically, it involves a complex series of events, including dilatation of arterioles, capillaries, and venules, with increased permeability and blood flow; exudation of fluids, including increased permeability and blood flow; exudation of fluids, including plasma proteins; and leukocytic migration into the inflammatory focus." Dorland's at 936.

Id.

Respondent filed an expert report from Dr. J. Lindsay Whitton, who is not a practicing clinician, but a virologist and pathologist, dated August 4, 2014. Ex. E (C.V. at Ex. E, Tab 1.) Dr. Whitton states that T.A.'s very rapid and profound rise in his neutrophil count is completely consistent with a bacterial infection. Ex. E, at 2. On August 24, 2011, T.A.'s proportion of neutrophils was higher than normal, but the absolute number of neutrophils was normal. Neutrophils are a type of white blood cell that combats bacterial infections. Id. at 1. T.A.'s wbc continued to rise extremely rapidly. Id. at 2. Sepsis can and in this case did very quickly lead to shock in which blood pressure declines and the blood supply to arms and legs is seriously compromised. Id. T.A. did not have encephalitis. T.A. did have encephalopathy. T.A. had a reduced level of consciousness because he was in shock. Id. Dr. Whitton states that culture-negative sepsis is very common. Id. at 3. Dr. Whitton states it can be extraordinarily difficult to grow bacteria in an artificial environment, resulting in a positive result only 50 percent of the time. Sepsis is a clinical diagnosis. Dr. Whitton said that T.A.'s fever, petechial rash, and thrombocytopenia were consistent with an MMR vaccine etiology, but were also consistent with sepsis. Id. at 4. Dr. Whitton states that the three attenuated viruses in MMR vaccine replicate to activate the immune response, which includes triggering cytokines. Id. Dr. Whitton states that the vast majority of viral infections do not cause cytokine storm. Id. at 5. He concludes that SIRS is more closely related to the innate immune response (occurring within two days of a trigger) than to the adaptive immune response. Id. at 6. Dr. Whitton disagrees with T.A.'s pediatrician Dr. Allen that MMR vaccine can cause an explosive increase in neutrophils 14 days after vaccination. Id. at 8.

Respondent filed a second supplemental expert report from Dr. Klein, dated August 19, 2014. Ex. F. He states if a vaccine were to induce SIRS, it would appear as anaphylaxis and immediately after the vaccination, not 13 days later as petitioners' expert Dr. Levin posited. Id. at 1. Dr. Klein states he has treated hundreds of cases of bacterial sepsis and T.A.'s onset, clinical course, and recovery are completely consistent with that diagnosis. Id.

Respondent filed a second supplemental expert report of Dr. Brown, which is undated. Ex. G. Dr. Brown states that "sepsis" refers only to a condition that bacterial infections cause. Id. at 1. Dr. Brown denies that MMR vaccine caused T.A.'s encephalopathy. Id.

Petitioners filed an expert report from Dr. David Axelrod, an immunologist, dated October 3, 2014. Ex. 24. He states that T.A. reacted to MMR vaccine 12 days after vaccination, with lethargy and fever, evolving to what became SIRS. Id. at 1. Dr. Axelrod writes that etiology of SIRS may be septic or non-septic. He states elevated levels of mannose-binding lectin ("MBL")[54] are associated with noninfectious SIRS with multiple organ failure, whereas low MBL is associated with multiple organ failure in infectious SIRS. Id. Dr. Axelrod says that

[54] Mannose-binding lectin is "a protein that is structurally similar to complement component C1 and recognizes many microorganisms, including bacteria, fungi, parasites, and viruses. It initiates the lectin pathway of complement activation, without the presence of antibody, by binding to carbohydrates on the microbial surface and activating C3." Dorland's at 1017.

T.A.'s MBL levels were high, suggesting T.A. had a noninfectious form of SIRS. Id. Moreover, T.A. suffered evidence of activation of the complement pathways with subsequent multiple organ failure as part of the SIRS. Id. at 3.

Respondent filed a supplemental expert report from Dr. Whitton, dated February 11, 2015. Ex. H. Dr. Whitton terms Dr. Axelrod's report "a series of unsubstantiated suppositions" and says Dr. Axelrod made "numerous errors of fact." Id. at 1. Dr. Whitton says that since MMR vaccine contains live vaccine, it is infectious. Id. at 2. Therefore, Dr. Axelrod makes no sense when he writes that T.A.'s SIRS had a noninfectious cause, yet was due to MMR vaccine. Id. He accuses Dr. Axelrod of failing to explain and/or misrepresenting the biological function of MBL. Dr. Whitton writes that MBL is a pattern recognition molecule that recognizes sugar-like structures present on the surfaces of some bacteria and viruses. Id. at 2. MBL is synthesized mainly in the liver and is readily detectable in most healthy people, usually above a level of ~1,000 µg/ml. Id. Dr. Whitton says measurement of MBL function, rather than level of MBL alone, may be a more reliable parameter to determine disease susceptibility. Id. at 2-3. MBL can sometimes rise in response to infection, but the rise is usually quite modest. Id. at 3. He notes that in a study of levels of MBL during sepsis in humans, the subjects had a relatively stable MBL level mostly. Id. Dr. Whitton says MBL appears to play a role in very early (innate) immune response to several infections. T.A.'s treating doctors were trying to see if T.A. had immunodeficiency when they tested his serum MBL levels, knowing he had a history of recurrent infectious. Id. Dr. Whitton noted that the two times T.A.'s MBL levels were tested, the results (1,384 µg/ml on September 9, 2011 and 522 µg/ml on November 14, 2011) were normal. But Dr. Whitton notes that the doctors did not evaluate T.A.'s MBL function. Id. Dr. Whitton states that having a high MBL is misleading because that number does not reflect an abnormality. Id. at 4. Dr. Whitton accepted that vaccination can cause transient fever and that fevers are cytokine-related. Id. at 6. Dr. Whitton explained the dramatic rise of T.A.'s blood neutrophil count indicated an acutely active process, rather than a delay of 12 days since MMR vaccination. Id. at 7. He states viruses associated with SIRS "cytokine storm" have the respiratory tract as a primary site of infection, but none of MMR vaccine's three viruses targets this tissue. Id.

Respondent filed a third supplemental report from Dr. Klein, dated February 19, 2015. Ex. I. He agrees with Dr. Whitton's report criticizing petitioner's expert Dr. Axelrod's report. Id. at 1. Dr. Klein states T.A.'s multi-organ failure was a result of bacterial sepsis. Id. Dr. Klein reiterates Dr. Whitton's point that since T.A. had a history of frequent staphylococcal infections, MBL tests were performed because MBL deficiency has been associated with recurrent infections. Id. at 2. Dr. Klein states that Dr. Axelrod's claim that a high level of MBL distinguishes between infectious and noninfectious causes is without foundation or recognition within the medical community. Id.

Petitioners filed a supplemental expert report from Dr. Levin, dated February 25, 2016. Ex. 43. Dr. Levin deals with timing in his supplemental report. Id. at 1. He states that T.A. received his first MMR vaccination on August 11, 2011 and it is well accepted that an initial immune response to measles vaccine usually takes weeks to develop. Id. Citing the numerous

attempts of T.A.'s hospital treaters to detect a bacterial infection by conventional cultures and PCR testing, Dr. Levin states their failure to find any bacterium makes it more probable than not that MMR vaccine caused T.A.'s SIRS. Id.

Respondent filed a third supplemental report from Dr. Brown, dated August 2, 2017. Ex. M. This was after the three-day hearing. He attributes all of T.A.'s clinical signs to likely "meningococcal encephalitis." Id. at 1. Both medication and infectious septic shock caused T.A.'s altered mental status. Id. Dr. Brown does not believe T.A. had acute encephalopathy persisting for 24 hours. Id. at 2. Lethargy, which T.A. had on September 25, 2011, is not evidence itself of an encephalopathy. When T.A. entered Mercy Hospital on September 25, 2011, he answered questions appropriately and responded to external stimuli until medication made him unresponsive and he entered a medically-induced coma. Id. Since T.A. recovered full consciousness and was fully responsive to his environment, he did not have a chronic encephalopathy for six months, although, to Dr. Brown, it is "possible" T.A. had an encephalopathy when he was septic, intubated, and struggling with multiple system issues as he was in acute multisystem organ failure that bacterial sepsis caused. Id. at 3. T.A. did not clearly have an acute encephalopathy for 24 hours before he was intubated. Id.

Petitioners filed a second supplemental report from Dr. Siegler, dated October 23, 2017. Ex. 55. Dr. Siegler posits that T.A. developed clinical signs of acute encephalopathy beginning on Tuesday, August 23, 2011 and before sedation the afternoon of Thursday, August 25, 2011. Id. at 1. He agrees with respondent's expert that T.A. had encephalitis, i.e., brain inflammation. Id. He states that T.A.'s brain inflammation was the likely pathologic process explaining T.A.'s encephalopathy. Dr. Siegler notes that on August 24, 2011, T.A.'s wbc and absolute neutrophil count were normal, when both are typically elevated in bacterial infections. Id. at 2. Dr. Siegler does not think T.A.'s answering questions appropriately at Mercy Hospital on August 25, 2011 rules out an acute encephalopathy because it can present as alternate levels of consciousness. Id. at 3. Dr. Siegler does not mention chronic encephalopathy in his report.

Respondent filed a fourth supplemental report from Dr. Brown, dated December 15, 2017. Ex. N. Dr. Brown states that he meant to write "meningococcal infection" in his third supplemental report, not "meningococcal encephalitis." Id. at 1.

Medical Articles

Respondent filed as Exhibit B, Tab 3, to his infectious diseases specialist Dr. Klein's expert report (Ex. B) chapter 64 from a medical text entitled NELSON TEXTBOOK OF PEDIATRICS (Robert M. Kliegman et al. eds.,19th ed. 2011), although the undersigned cannot find in Dr. Klein's report that he referred to it: David A. Turner[55] & Ira M. Cheifetz,[56] Shock, 305-14. Ex.

[55] Dr. David A. Turner is Associate Director, Pediatric Critical Care Fellowship Program; Medical Instructor, Department of Pediatrics, Division of Pediatric Critical Care Medicine, Duke University Medical Center, Durham, North Carolina. Contributors, NELSON TEXTBOOK OF PEDIATRICS xxx (Robert M. Kliegman et al. eds., 19th ed. 2011).

[56] Dr. Ira M. Cheifetz is Professor of Pediatrics; Chief, Pediatric Critical Care Medicine; Medical Director, Pediatric

B, Tab 3. The authors write under the subheading "Pathophysiology" the following:

> An initial insult triggers shock, leading to inadequate oxygen delivery to organs and tissues. Compensatory mechanisms attempt to maintain blood pressure by increasing cardiac output and systemic vascular resistance. The body also attempts to optimize oxygen delivery to the tissues by increasing oxygen extraction and redistributing blood flow to the brain, heart, and kidneys (at the expense of the skin and gastrointestinal tract). These responses lead to an initial state of compensated shock, in which blood pressure is maintained. If treatment is not initiated or is inadequate during this period, decompensated shock develops with hypotension and tissue damage that may lead to multisystem organ dysfunction and ultimately to death. . . .

Id. at 2 (internal page 305).

The authors also define SIRS:

> The systemic inflammatory response syndrome (SIRS) is an inflammatory cascade that is initiated by the host response to an infectious or noninfectious trigger (Table 64-5). This inflammatory cascade is triggered when the host defense system does not adequately recognize and/or clear the triggering event.

Id. at 4 (internal page 307). Table 64-5, to which this excerpt refers, is entitled, "Differential Diagnosis of Systemic Inflammatory Response Syndrome." Id. at 6 (internal page 309). Included in the sub-category "Infection" are the following:

> **Bacteremia or meningitis** (*Streptococcus pneumoniae*, *Haemophilus influenza* type b, *Neisseria meningitidis*, group A *streptococcus*, *S. aureus*)
> **Viral Illness** (influenza, enteroviruses, hemorrhagic fever group, herpes simple[x] virus, respiratory syncytial virus, cytomegalovirus, Epstein-Barr virus)
> **Encephalitis** (arboviruses, enteroviruses, herpes simplex virus)
> **Rickettsiae** (Rocky Mountain spotted fever, *Ehrlichia*, Q fever)
> **Syphilis**
> **Vaccine reaction** (pertussis, influenza, **measles**)
> **Toxin-mediated reaction** (toxic shock, staphylococcal scalded skin syndrome)

ICU; Medical Director, Pediatric Respiratory Care & ECMO Programs, Duke Children's Hospital, Durham, North Carolina. Contributors, NELSON TEXTBOOK OF PEDIATRICS x (Robert M. Kliegman et al. eds., 19th ed. 2011).

Id. (emphasis added). The authors also add other causes of SIRS under separate sub-categories: cardiopulmonary, metabolic-endocrine, gastrointestinal, hematologic, neurologic, and other. Id.

This chapter on shock in the well-recognized NELSON TEXTBOOK OF PEDIATRICS supports the view that the pediatric medical community considers one of the causes of SIRS is a reaction to measles vaccine.

Petitioners' counsel referred to the same chapter's Table 64-7 in cross-examination of Dr. Whitton. Table 64-7 is on page 8 of Ex. B, Tab 3 (internal page 311):

Table 64-7 – INTERNATIONAL CONSENSUS DEFINITIONS FOR PEDIATRIC SEPSIS	
Infection	Suspected or proven infection or a clinical syndrome associated with high probability of infection
Systemic inflammatory response syndrome (SIRS)	2 out of 4 criteria, 1 of which must be abnormal temperature or abnormal leukocyte count: 1. Core temperature >38.5˚C or <38˚C (rectal, bladder, oral, or central catheter) 2. Tachycardia: Mean heart rate >2 SD above normal for age in absence of external stimuli, chronic drugs or painful stimuli *OR* Unexplained persistent elevation over 0.5-4 hr *OR* in children <1 year old, persistent bradycardia over 0.5 hour (mean heart rate <10th percentile for age in absence of vagal stimuli, ß-blocker drugs, or congenital heart disease) 3. Respiratory rate >2 SD above normal for age or acute need for mechanical ventilation not related to neuromuscular disease or general anesthesia 4. Leukocyte count elevated or depressed for age (not secondary to chemotherapy) or >10% immature neutrophils
Sepsis	SIRS plus a suspected or proven infection
Severe Sepsis	Sepsis plus 1 of the following: 1. Cardiovascular organ dysfunction, defined as: •Despite >40 mL/kg of isotonic intravenous fluid in 1 hour: •Hypotension <5th percentile for age or systolic blood pressure <2 SD below normal for age *OR* •Need for vasoactive drug to maintain blood pressure *OR* •2 of the following: •Unexplained metabolic acidosis: base deficit >5 mEq/L; •Increased arterial lactate: >2 times upper limit of normal; •Oliguria: urine output <0.5 mL/kg/hr; •Prolonged capillary refill: >5 sec; •Core to peripheral temperature gap >3˚C 2. Acute respiratory distress syndrome (ARDS) as defined by the presence of a $PaO_2/F10_2$ ratio ≤300 mm Hg, bilateral infiltrates on chest radiograph, and no evidence of left heart failure *OR* Sepsis plus 2 or

	more organ dysfunctions (respiratory, renal, neurologic, hematologic, or hepatic)
Septic shock	Sepsis plus cardiovascular organ dysfunction as defined above
Multiple organ dysfunction syndrome (MODS)	Presence of altered organ function such that homeostasis cannot be maintained without medical intervention

Respondent filed as Exhibit C, Tab 1, to Dr. Brown's supplemental expert report (Ex. C) the following medical article: Derek C. Angus & Tom van der Poll, Severe Sepsis and Septic Shock, 369 N ENGL J MED 9:840-51 (2013). The authors state that "signs of a systemic inflammatory response, such as tachycardia or an elevated white-cell count, occur in many infectious and noninfectious conditions . . . ." Id. at 840. This medical article supports the view that the medical community accepts non-infectious causes of SIRS.

Respondent filed as Exhibit C, Tab 2, the following untitled chapter from RED BOOK: 2009 REPORT OF THE COMMITTEE ON INFECTIOUS DISEASES (Larry K. Pickering et al. eds., 28th ed. 2009) (missing internal page numbers, but respondent numbered pages 1-6). The authors state in the category of adverse events a fever of 103 degrees or higher occurring between 6-12 days after MMR vaccination. Id. at 4. Transient rashes and thrombocytopenia have been reported. Id. Thrombocytopenia has occurred between two to three weeks after MMR vaccination. Id. at 5. This report supports the view that reactions of fever, rash, and thrombocytopenia occur at least almost a week or two after MMR vaccination.

Respondent filed as Exhibit E, Tab 2, to Dr. Whitton's expert report (Ex. E) the following medical article: Jason Phua et al., Characteristics and outcomes of culture-negative versus culture-positive severe sepsis, 17 CRITICAL CARE R202 1-12 (2013) doi:10.1186/cc12896. Although bacteria are known to cause 50 percent of severe sepsis cases, less is known about the other half of severe cases for which etiologic agents have not been discovered. Id. at 1. The authors state that "severity of illness and mortality are not significantly affected by microbiological documentation in sepsis. . . ." Id. They posit that some of the culture-negative

sepsis patients might have had nonbacterial sepsis. Id. at 9. They also consider that some of these patients might not have had actual sepsis. Id. This article supports the view that nonbacterial sepsis may be just as severe as bacterial sepsis.

Respondent filed as Exhibit E, Tab 6, to Dr. Whitton's expert report (Ex. E) the following medical article: Steven D. Burdette, Systemic Inflammatory Response Syndrome, MEDSCAPE (updated: Jan. 29, 2014) https://emedicine.medscape.com/article/168943-overview (last visited July 23, 2018).[57] The author states that "SIRS is not always related to infection." Id. at 1. He also states, "Although not universally accepted terminology, severe SIRS and SIRS shock are terms that some authors have proposed. These terms suggest organ dysfunction or refractory hypotension related to an ischemic or inflammatory process rather than to an infectious etiology." Id. at 2. The author states, "Systemic inflammatory response syndrome (SIRS), independent of the etiology, has the same pathophysiologic properties, with minor differences in inciting cascades. Many consider the syndrome a self-defense mechanism. Inflammation is the body's response to nonspecific insults that arise from chemical, traumatic, or infectious stimuli." Id. The author lists as one of the noninfectious causes of SIRS: "drug reaction." Id. at 4. The author states, "Of the SIRS patients without infection, the clinical characteristics were similar to those with positive cultures." Id. at 5. This medical article supports the view that the medical community accepts that non-infectious causes such as drug reaction can cause SIRS and the clinical characteristics of SIRS do not differ whether the cause is infectious or non-infectious.

Respondent filed as Exhibit E, Tab 7, to Dr. Whitton's expert report (Ex. E) pages 75-76 from a chapter entitled "Evaluating Biological Mechanisms of Adverse Events" and a subchapter entitled "Immune-Mediated Mechanisms," and pages 218-21 from the book ADVERSE EFFECTS OF VACCINES. EVIDENCE AND CAUSALITY (Kathleen Stratton et al. eds., 2012). This excerpt from the Institute of Medicine ("IOM") states subtle imbalances of proinflammatory and anti-inflammatory cytokines may follow immunization against rubella, citing four medical articles. Id. at 76. Moreover, the IOM considered that a vaccinee's unique immunogenetic makeup might predispose him to an exaggerated cytokine imbalance following immune stimulation such as vaccine administration. Id. The IOM took a neutral stance as to whether or not vaccinations can result in oversecretion of cytokines. Id.

Respondent filed as Exhibit H, Tab 4, to Dr. Whitton's supplemental expert report (Ex. H) the following medical article: Damon P. Eisen & Robyn M. Minchinton, Impact of Mannose-Binding Lectin on Susceptibility to Infectious Diseases, 37 CLIN INFECTIOUS DIS 1496-1505 (2003). The authors show that low mannose-binding lectin ("MBL") is related to greater risk of infection. In discussing *Neisseria meningitidis*, the authors state MBL stimulates phagocytosis of this disease by neutrophils, macrophages, and monocytes, and increases the rate of killing of the organism while modulating the immune response through reduced production of proinflammatory cytokines. Id. at 1499. T.A.'s doctors tested T.A.'s MBL levels to find out if

[57] Respondent did not provide an electronic citation for this 2014 version. The updated version is dated May 7, 2018 and the author is Lewis J. Kaplan. Petitioners filed the same article as Exhibit 41 but updated to Mar. 30, 2015 with the author as Lewis J. Kaplan and the same electronic citation the undersigned notes in the text of this opinion. Petitioners' and respondent's pagination are identical, and the undersigned cites this pagination.

he were deficient since he had a history of staphylococcal infections. T.A.'s levels were not deficient.

Petitioners filed as Exhibit 36 an excerpt from CENTERS FOR DISEASE CONTROL AND PREVENTION. EPIDEMIOLOGY AND PREVENTION OF VACCINE-PREVENTABLE DISEASES (Jennifer Hamborsky et al. eds., 13th ed., 2015). The CDC state:

> The immune response to a live attenuated vaccine is virtually identical to that produced by a natural infection. The immune system does not differentiate between an infection with a weakened vaccine virus and an infection with a wild virus.

Id. at 5 (petitioners' page 16).

Petitioners filed as Exhibit 44 to Dr. Levin's supplemental expert report (Ex. 43) the following medical article: Rita F. Helfand et al., Timing of Development of Measles-Specific Immunoglobulin M and G after Primary Measles Vaccination, 6 CLIN DIAGN LAB IMMUNOL 2:178-80 (1999). The authors tested 209 children to determine when, after measles vaccination, they had the greatest positive IgM results. Id. at 178. The answer was the second and third weeks after measles vaccination. Id. This article supports the opinion that immunity after measles vaccination takes two to three weeks to develop.

TESTIMONY

Before testimony began, the undersigned had a discussion on the record with counsel during which respondent's counsel stated there was an issue of more than six months of sequelae should the undersigned rule in favor of petitioners. Tr. at 6-7. The undersigned explained for the benefit of the petitioners sitting in the hearing room that this discussion was in the context of petitioners' proving a Table acute encephalopathy which must be followed by a chronic encephalopathy lasting more than six months and proving a Table thrombocytopenic purpura which must be followed by more than six months of sequelae. Id. at 9. In addition, petitioners were alleging causation in fact SIRS. Id. The undersigned said that if the undersigned ruled MMR vaccine caused in fact T.A.'s SIRS, no one was going to doubt there were more than six months of sequelae. Id. at 9.

Petitioner Mr. Ahlum testified first. Tr. at 41. T.A. received MMR vaccine on August 11, 2011. Id. at 45. T.A. started getting sick on Tuesday, August 23, 2011 because he had a fever. Id. at 46. No one else in the family was ill. Id. His wife called the pediatrician and the staff recommended using Tylenol and ibuprofen and scheduled an appointment with Dr. Allen the next morning. Id. at 47. T.A. was a little irritated. Id. at 48. When T.A. came home from seeing Dr. Allen, T.A. was worse. Id. at 50. In the late evening, he was throwing up and had diarrhea. Id. T.A. was lethargic, and defecated in his pants. Id. at 51. Dr. Allen called an ambulance to start IVs on the way to Mercy Hospital. Id. at 52. Dr. Allen cleared his schedule for the rest of the day. Id. at 53. T.A. perked up with the IV fluid and said he wanted something

to drink and maybe watch a little television. Id. at 54. T.A. became much worse and plans were made around 4:00 or 5:00 p.m. to airlift him to Arkansas Children's Hospital. Id. at 55. The anesthesiologist came in to intubate T.A. and put him to sleep. Id. T.A. freaked out and was scared. Id. at 56. To Mr. Ahlum, it looked as if T.A. was essentially doing okay; he was still breathing fine. Id. Dr. Allen was really concerned about T.A.'s insulin level. Id.

When the staff at Arkansas Children's Hospital finally let Mr. Ahlum into T.A.'s room around 11:30 p.m., T.A. had multiple tubes in him and he was leaking fluids out of every orifice. Id. at 58. None of the staff was wearing a mask and he was not either. Id. He was with T.A. every night for the weeks T.A. was at Children's. Id. at 60. There was not a moment that someone in the family was not at his bedside. Id. Immediately after the hospital discharged T.A., it readmitted him the next day. Id. This readmission lasted one week and T.A. was with his mother because Mr. Ahlum went back to work with Mr. Ahlum visiting on the weekends. Id. at 60-61. As Mr. Ahlum put it, T.A. did "some crazy things." Id. T.A. would stand up on his stumps, run on his bed, try to jump off, and lash out at his mother. Id. That behavior continued in the weeks after petitioners and T.A. returned home. It felt as if T.A. were possessed. He was "just completely out of his mind on many occasions." Id. When T.A. went back to Dr. Allen's clinic, it was "a life-altering experience for everyone in their clinic." Id. at 62. They had a cake for him and nice things, but it was a terrible experience. Id. at 63. T.A. was angry that it was happening and he destroyed the cake in front of everyone. Id. T.A. had no eye contact. He would look around with just a dead stare. Id. Before all this happened, T.A. was the life of the party for himself and his older brother. Id. at 64. That was no longer T.A. after this experience. Id. Also, after this experience, T.A. was no longer potty trained. Id. at 65. When Thanksgiving came, T.A. was off in his little room. Id. It broke Mr. Ahlum's mother's heart. Id.

Mr. Ahlum said T.A. hated to go to therapy. Id. at 67. He does pretty well in school. Id. He has home school two days a week and goes to a private school two days a week. Id. at 68. T.A.'s reading level is a grade behind. Id. T.A. puts things in his mouth, like his T-shirt edge or a Lego. Id. at 69. He does not want to go outside and play, and he mutters. Id. at 70. Early on, T.A. was having "unbelievably terrible night terrors." Id.

Dr. Barry Allen, T.A.'s treating pediatrician, testified next. Id. at 104. He has been in practice since 1976, or 40 years at the time of the hearing. Id. at 105. T.A. received his first MMR vaccination on August 11, 2011. Id. at 107, 108. Dr. Allen next saw T.A. 13 days later on August 24, 2011, because T.A. had fever and a rash. Id. at 108. T.A. had a fever of 102 degrees and a petechial rash. Id. T.A. also had a macular rash on his neck and trunk. Id. at 109. His white blood cell count was 6,000, which is normal. His platelet count was low. Dr. Allen gave T.A. Rocephin. Id. When the undersigned asked Dr. Allen what was the difference between a macular rash and a petechial rash, he replied a macular rash is a red rash and a pectechial rash little blood spots on the skin. Id. Dr. Allen gave T.A. an antibiotic because he was concerned that T.A. could have an infection because of his low platelet count and fever. Id.

Dr. Allen has had patients who had an adverse reaction to MMR vaccine. Id. at 110. The typical time frame after vaccination was a week to several weeks. Id. T.A. returned to Dr. Allen

the next day, on August 25, 2011, and was very seriously ill. Id. He was 10 percent dehydrated and had vomited during the night. Id. His platelet count had dropped to 73,000. Id. at 110-11. His white blood cell count had risen from 6,000 to 20,000. Id. at 111. Dr. Allen's concern was to get T.A. out of a shock-like state. He started an IV on T.A. in the office and transferred him to the hospital and then to Arkansas Children's Hospital. Id. Dr. Allen considered the diagnostic possibilities to be sepsis and thus putting T.A. on IV fluids and IV antibiotics, but also T.A. could be reacting to MMR vaccination because of the time interval. Id. He went in the ambulance with T.A. to the hospital. Id.

During T.A.'s time at Arkansas Children's Hospital, T.A. was on multiple antibiotics, on medication to maintain his blood pressure, and on dialysis. Id. at 112. T.A. had multiple blood tests, multiple cultures, and PCRs to identify a bacterial cause, and the results were all negative. Id. Rocephin is a broad-based antibiotic that covers meningococcus, pneumococcus, and streptococcus. Id. It works within minutes to hours. Id. at 113. T.A. did not improve after being on Rocephin. Id. In light of the failure of the cultures and PCR to find a bacterial cause, Dr. Allen reassessed the timing of the MMR vaccination considering the onset of T.A.'s illness. Id. Dr. Allen testified, "I have thought about him obviously several times over the past years, and I have to think that the MMR was the etiology of his illness." Id.

When Dr. Allen saw T.A. on October 24, 2011, T.A. had not returned to his neurological baseline because he still did not make eye contact or smile, and this was a week after he was discharged from the hospital. Id. at 114. He also had some aggressive behavior. Id. It could indicate depression and even some neurological problems. Id. T.A. has not received a second MMR vaccination. When asked if he would recommend T.A. receive a second MMR vaccination, Dr. Allen replied, "Well, that would be a very difficult decision for me. I would probably recommend the other immunizations, but I would be very reluctant to recommend an MMR for T.A." Id.

On cross-examination, Dr. Allen agreed that the standard of care for a patient with bacterial sepsis is the administration of antibiotics and when he saw T.A. on August 24, 2011, he suspected T.A. had a possible bacterial infection. Id. at 115. Dr. Allen admitted he is not an infectious diseases specialist. Id. at 118. He also admitted that a macular rash and a petechial rash can indicate an infectious process, including meningococcus. Id. at 120. T.A.'s symptoms were consistent with a meningococcal infection. Id. at 124. Dr. Allen's initial concern on August 24, 2011 was sepsis, but T.A. did not have purpura. Id. Dr. Allen said that his records do not reflect his considering a reaction to MMR because he was primarily concerned initially about an infection, but the fact that T.A. had MMR only came to light later. Id. He did not note it in his record for August 25, 2011 because T.A. was very ill, dehydrated, and hypovolemic. Id. at 125. He does not know why he did not dictate the role of MMR vaccine when he wrote the discharge summary at Mercy Hospital. Id. After T.A. was transferred to Arkansas Children's Hospital, Dr. Allen went back and looked through T.A.'s record and became aware that he had received MMR vaccine. Id. at 126. Dr. Allen said, "We were trying to save his life at the time he was transferred, Ma'am." Id. Dr. Allen did, after the initial day, have phone conversations with the doctors at Arkansas Children's Hospital. Id. It does not surprise Dr. Allen that his

phone conversations with the doctors at the hospital are not reflected in their records. Id. at 128. He does remember telling the doctors that T.A. had received MMR vaccine two weeks before. Id. He is aware that except for a reference in the hospital records to SIRS, the diagnosis throughout the other records at Arkansas Children's Hospital is to bacterial shock and sepsis. Id. at 129. Dr. Allen stated again that his focus on MMR vaccine as the cause was the two-week interval between vaccination and T.A.'s illness, and the negative results of the PCRs and cultures. Id. at 132. Dr. Allen never diagnosed T.A. as having encephalopathy. Id. at 133-34.

Petitioner Mrs. Ahlum testified next. Id. at 143. After T.A. received MMR vaccine on August 11, 2011, he was fine the week afterwards. Id. at 145. On Monday, he was tired. On Tuesday, he ran a low-grade fever in the morning. He was tired. Later in the evening, he ran a higher temperature. She called the local walk-in clinic and the nurse told her to use ibuprofen and Tylenol, and to see the doctor in the morning. Id. at 145. On August 24, 2011, she took him to Dr. Allen. Id. at 146. T.A. had a 102 fever, a small pinpoint rash plus another kind of rash, low platelets, and was very sick. Dr. Allen gave him a shot of Rocephin and told them to come back the next day. Id. That night, T.A. got worse. He started throwing up and had diarrhea. Id. They went back to Dr. Allen earlier than their appointment and T.A. was lethargic. Id. at 147. T.A.'s platelets were lower and his white blood cell count was higher. She rode in the ambulance with T.A. and Dr. Allen. Id. T.A. seemed to perk up in Mercy Hospital, but his insulin level started skyrocketing to 400 and then to 661. Id. at 148. The doctors thought T.A. was going into diabetic shock. Then T.A. started crashing. Id. No one in T.A.'s room including her and her four-month-old baby wore protective garb to protect them from a virus or bacterium. Id. at 149.

When Mrs. Ahlum arrived at Arkansas Children's Hospital, T.A. was in the PICU and not isolated from anyone else. Id. at 150. The only time personnel were really concerned about wearing a mask was after T.A.'s legs turned purple and were blistered and the Burn Team came in to make sure his legs did not get infected. Id. at 151. The next day, Mrs. Ahlum told two infectious diseases doctors that the family had gone to a petting zoo at the state fair and she had washed T.A.'s hands and put antibacterial spray on them. Id. at 151. The doctors had no idea what the cause of T.A.'s illness was. Id. at 152.

Dr. Alan S. Levin testified next for petitioners. Id. at 175. He is board-certified in allergy, immunology, pathology, and emergency medicine. Id. at 178. He is a member in the American Academy of Allergy, Immunology. Id. He used to teach medical students medicine and immunology. Id. at 179. He testified he is very familiar with vaccines in general and the immunology of vaccines. Id. at 180. He has treated about a hundred patients with SIRS. Id. He spends about 95 percent of his time working as a lawyer. Id. at 183. The other five percent of time he treats patients. Id. Since 1993, the majority of his time has been spent practicing law. Id. at 184. He practices toxic torts. Id. at 185. He became a lawyer because "toxic tort litigation is the single-most powerful tool to advance science." Id. at 186. Respondent did not object to Dr. Levin as an expert in immunology. Id. at 196.

Dr. Levin testified that when T.A. saw Dr. Allen on August 11, 2011, he did not have an

infection when he received MMR vaccine. Id. at 198. Dr. Levin said that an adverse reaction to MMR vaccine is very rare. Id. at 198-98. He stated measles virus is not very pathogenic compared to influenza. Id. at 199. MMR does not have enough of the receptor molecules on the cell surface to provoke the immune system. Id. Killed measles virus vaccine did not work. Then the manufacturers created attenuated measles virus vaccine so that it could replicate, but it did not replicate as quickly and aggressively as wild measles virus. Id. The attenuated measles virus vaccine is safer than having wild measles, but it does not provoke an immune response as rapidly as wild measles virus. Id. at 199-200. The immune response that the attenuated measles virus provokes in a naïve patient, i.e., one who has not received measles vaccine before such as T.A., takes roughly two weeks to have an immune response. Id. at 200. Although the attenuated measles virus vaccine provokes the innate immune system a little bit, Dr. Levin said the vaccine primarily reacts against the adaptive immune system. Id.

Dr. Levin explained that the innate immune system recognizes patterns of molecules and serves as a gate guard. Id. It is the original protector of the body and responds within hours. The adaptive immune system functions by having receptors identify the tertiary structure of an antigen. Molecules signal the cells to secrete antibodies or cytokines. The adaptive immune system responds in weeks. Respondent's experts ask why T.A. did not become ill in the first 48 hours after his MMR vaccination. The answer is that the vaccination did not provoke the innate immune system enough to cause him to be sick. Id. After two weeks, then the adaptive immune system starts working against the vaccine and we see the cytokine storm that T.A. suffered. Id. at 201. Dr. Levin cited the Helfand article (Ex. 44) as support for at least a week or two weeks before an immunological response to a first MMR vaccination occurs. Id. at 203.

Dr. Levin explained SIRS. Id. at 204. People have only a few ways of responding to an immunologic insult. SIRS is the way that people respond to bacteria, viruses, fungi, toxic chemicals, and vaccines. Id. Once SIRS is triggered, it goes on spontaneously in the body as happened in T.A. Id. In SIRS, there is an overreaction of pro-inflammatory or anti-inflammatory cytokines and other agents that cause inflammatory response. Id. at 205. Certain molecules, such as interleukin-6 and sometimes interleukin-1, can reach endothelial cells or the cells that bind capillaries of the blood vessels and cause the cells that have fused together to separate. Then plasma comes out and causes edema, which happened in T.A.'s arms and probably in his brain. Id. Edema causes all kinds of problems in the central nervous system and circulation. Then there is clotting of blood, platelets sticking together, intervascular coagulation, and thrombocytopenia in which the level of platelets decreases, causing blood clots, which happened to T.A.'s legs. The reason the legs are vulnerable is they are far from the heart and they die first. Id. Interleukin-1 and Interleukin-6 are small protein molecules secreted by macrophages primarily and increase inflammation. Id. at 205-06. Although it is called an immune system, Dr. Levin prefers to call it a system of growth and differentiation, i.e., part of the system destroys and the other part of the system heals. Id. at 206. Dr. Levin said life is homeostasis.[58] Id. In T.A.'s case, it was the pro-inflammatory cytokines that caused the harm. Id. T.A.'s maculopapular rash, petechial rash, 103 degree fever, vomiting, and diarrhea were

[58] Homeostasis is "a tendency to stability in the normal body states (internal environment) of the organism. It is achieved by a system of control mechanisms activated by negative feedback. . . ." Dorland's at 867.

consistent with a reaction going out of control. Id. at 208-09. Those symptoms are what make the reaction systemic. Id. at 209.

In Dr. Levin's opinion, T.A.'s fever on August 23, 2011 was due to MMR vaccination. Id. The pro-inflammatory cytokines triggered T.A.'s fever. Id. Dr. Levin said that T.A.'s white cell count rising from 6,000 on August 24, 2011 to 20,000 on August 25, 2011 was very typical of a SIRS reaction to bacteria, viruses, toxic chemicals, and/or vaccines. Id. at 210. The spleen "spits out" all kinds of cells. Id. T.A.'s decrease in platelet counts from 97,000 on August 24, 2011 to 73,000 on August 25, 2011 were partially responsible for the petechial rashes and little blood clots, and were also a response to MMR vaccine. Id. Dr. Levin said that because T.A.'s titers were positive to measles, he had a local reaction which was the predicate of a systemic reaction to the vaccine. Id. at 212-13. The local reaction is a good thing, not an adverse reaction. Id. at 214. Dr. Levin said that the adaptive immune system can cause SIRS and did so in T.A. Id. at 215. The appropriate time for a SIRS reaction is one to three weeks post-vaccination. Id.

Dr. Levin noted that, although T.A. received the antibiotic Rocephin on August 25, 2011, the antibiotic did not work and T.A. became much sicker. Id. at 216. The failure of Rocephin to help T.A. mitigates against T.A. having a bacterial infection that caused his SIRS. Id. at 216-17. Dr. Levin stated that meningococcus is exquisitely sensitive to Rocephin and the failure of Rocephin to work means T.A. probably did not have meningococcus. Id. at 217. In T.A.'s case, the most probable cause of T.A.'s SIRS was the MMR vaccine because the doctors could not find a pathogen. Id. at 219. Dr. Levin said that the immunology unit of the Arkansas Children's Hospital is one of the best immunology units in the United States. Id. at 220.

Dr. Levin said that all SIRS is the same, whether the trigger is bacteria or a vaccination. Id. at 224. He said humans have a limited repertory of responses to insults. Id. Dr. Levin called NELSON TEXTBOOK OF PEDIATRICS (Ex. B, Tab 3) the bible of pediatrics. Id. at 225. The chapter from NELSON that respondent filed as an exhibit lists measles vaccine as a cause of SIRS. Id. at 223-24. The chapter includes measles vaccine as part of its list of infections. Dr. Levin said that since attenuated measles vaccine replicates, measles virus vaccine is an infection. Id. at 225. SIRS leads to sepsis by replicating an infectious organism causing a disease process. Id. at 227. T.A. had a fever, tachycardia, respiratory distress, elevated neutrophils, all indicative of SIRS on August 25, 2011. Id. at 228. Elevated neutrophils are not indicative of bacterial infection; rather they are a criterion for SIRS no matter what the cause. Id.

Dr. Levin's opinion is that T.A. had SIRS which MMR vaccine probably triggered. Id. at 236. He also believes that T.A. did not have meningococcus because Rocephin did not help T.A. get better. Id.

On cross-examination, Dr. Levin agreed that *Neisseria meningitidis* is a very infectious disease process.[59] Id. at 255. It is one of the most common causes of SIRS. Id. at 256. On

[59] The undersigned recalled Mrs. Ahlum to testify if she or her baby got sick since they were purportedly exposed to what respondent's experts and Dr. Levin agreed is a very infectious disease process. The undersigned asked Mrs.

redirect, Dr. Levin noted that T.A. also had a nasal culture which was negative. Id. at 263. Dr. Levin thinks that T.A.'s having a staph infection on his neck which formed a cyst and had to be drained when he was an infant is relevant because T.A. may have had some immune dysregulation prior to being vaccinated against MMR in 2011. Id. at 267. Dr. Levin said that T.A. had an immune workup after his SIRS, which indicated a very subtle immune dysregulation. Id. at 268. Whether or not T.A. has an immune deficiency does not affect Dr. Levin's opinion that MMR vaccine caused T.A.'s SIRS. Id. at 302.

Dr. David Siegler testified next for petitioners. Id. at 304. He is a pediatric neurologist. Id. at 305. He is familiar with how MMR vaccine initiates the immune response. Id. at 314. The three viruses making up the vaccine are attenuated, i.e., engineered to be less virulent. Once injected in the recipient, the viruses replicate but not to the degree that a live, wild virus would. The viral replication induces the immune system to develop a response to produce immunity. Id. Twelve days after T.A. received MMR vaccine, he had symptoms. Id. An adverse reaction to MMR takes days because the immune response needs to gear up. Id. at 315. The Vaccine Injury Table puts the Table duration as five to 15 days. Id. T.A.'s having fever 12 days after MMR vaccination followed by the other symptoms fits perfectly in the timing of what is expected for an adverse reaction to MMR vaccine. Id. The adverse reaction is systemic, causing inflammation which can affect all organs. Id. at 316. On August 24, 2011, T.A. saw Dr. Allen and had a fever of 102 degrees, petechial rash over his neck and trunk, macular rash on his trunk, low platelet count, and a normal white blood cell count. Id. at 317. The low platelet count can be caused by either MMR vaccine or inflammation resulting in clotting. Id.

Dr. Siegler said that Rocephin administered intramuscularly works quickly on a bacterial infection. Id. at 319. The Rocephin did not work which means either T.A. did not have a bacterial infection or the antibiotic was not the correct one to use. Id. at 320. Dr. Siegler said that on August 25, 2011, T.A. was manifesting signs and symptoms of encephalopathy. Id. at 322. T.A. was quite lethargic, meaning he had a depressed level of consciousness, which is a sign of encephalopathy. Id. T.A. was so depressed in consciousness that he had no normal response to his need to defecate and stooled in his pants. Id. at 323. Dr. Siegler said T.A.'s decreased level of consciousness lasted more than 24 hours. Id. He said T.A.'s change in mental status was not related to medication. Id.

Dr. Siegler's opinion is that T.A. had an adverse reaction to MMR vaccine. Id. at 337. There was no other explanation and he did not improve on the various antibiotics he received. Id. at 338. Dr. Siegler agrees with the diagnosis of SIRS. Id. Dr. Siegler believes that T.A.'s behavioral peculiarities are due to his acute encephalopathy. Id. at 342. He thinks T.A.'s petechiae were due to his low platelet count from his MMR reaction and the macular rash was due to the MMR reaction. Id. at 348. Dr. Siegler said that the first neurologic symptom in shock regardless of the cause is poor perfusion which leads to a depressed level of consciousness. Id. at 366. Then comes ischemia, cranial nerve dysfunction, edema, bleeding, and possible strokes

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Ahlum if, after the night between August 24 and 25, 2011, when she had T.A. in bed with her on one side and her four-month-old baby on the other side, and T.A. was vomiting and had diarrhea all night, if she or her four-month-old baby got sick. She said no. Id. at 304.

and seizures. Id. at 367. Ischemia is decreased blood flow that can cause tissue injury due to lack of nutrients or oxygen to an area. If blood flow is diminished too long to the extremities, necrosis occurs. Id. In the hospital, doctors had to give T.A. pressors to increase his blood pressure and get blood moving to his brain. Id. at 368. Muscles have a greater metabolic demand for nutrients and oxygen which is why T.A.'s leg muscles died before his skin. Id. T.A.'s kidneys shut down and he was on dialysis, but the kidneys came back. Id. T.A.'s liver function tests were very elevated. Id. at 369. Dr. Siegler explained that a depressed level of consciousness means that the brain is impaired. Id. at 370.

Dr. Siegler's opinion is that T.A. had an adverse reaction to MMR that presented initially with fever and petechiae, followed by encephalopathy. Id. at 374. T.A.'s first symptoms were a systemic inflammatory event that ultimately resulted in multi-organ dysfunction, the earliest being brain dysfunction or encephalopathy from a depressed level of consciousness. Id. The initial reaction to MMR vaccine was begun in the immune system and, in the course of that immunologic reaction, he had symptoms of encephalopathy. Id. The first signs of T.A.'s reaction to MMR occurred on August 23, 2011 with fever and rash. Id. at 377. He was not encephalopathic at the time. Id. T.A. did not have a consultation with a neurologist. Id. at 383. Dr. Seigler said that T.A.'s encephalopathy began on August 25, 2011. Id. at 386. When T.A. arrived at Mercy Hospital, he perked up and wanted lemonade and to watch cartoons, meaning his encephalopathy was improved. Id. at 389. Prior to T.A.'s transport by helicopter, he was intubated at 4:30 p.m. and sedated at 4:25 or 4:30 p.m. at Mercy Hospital. Id. at 386, 408, 409.

Dr. J. Lindsay Whitton testified next for respondent. Id. at 440. He is a full professor at the Scripps Research Institute working on the immune response to viral and bacterial infections. Id. at 441-42. He also works on vaccines. Id. at 442. He studies the interface between viruses and immunology in live animals. He infects animals with viruses and studies how their immune systems respond to the viruses. Id. Dr. Whitton does not have patients. Id. at 442-43. His funding come from National Institutes of Health grants. Id. at 444. He is an editor of the journal Virology. Id. at 449. Essentially all of his work relates to the immune system and how viruses and/or bacteria cause disease. Id. at 452-53. He works on Group B streptococcus and *Staphylococcus aureus*. Id. at 453. He does not work on fungi in the lab. Id. at 454. When he works with rats, rabbits, and mice, he is trying to induce an inflammatory response by introducing either a virus or a bacterium. Id. Dr. Whitton has not ever qualified to practice medicine in the United States because he wanted to do research. Id. at 464.

Dr. Whitton said the immune system is smart enough to recognize the type of invader of a bacterium or a virus and then mount the type of immune response that is best suited to deal with the invader. Id. at 455. Dr. Whitton has done research on vaccines. Id. at 457. He does not work on measles in the lab because it is hard to get a great animal model for measles. Id. at 458.

Dr. Whitton said that T-cells help to control viral infection by secreting cytokines. Id. at 460. Cytokines are very toxic molecules and dangerous. Id. Whereas antibodies recognize free viruses floating in the blood, T-cells recognize intact cells that are infected with viruses. Id. T-

cells make cytokines which are in direct contact with the virus-infected cell and, after direct contact, the T-cell shuts down cytokine production. Id. at 461. There is a constant balance between pro-inflammatory and anti-inflammatory cytokines. Id. at 462. When things get out of control, there is cytokine storm. Id. at 463.

Dr. Whitton said that measles is a viral infection. Id. at 465. Dr. Whitton's opinion is that MMR vaccine did not play any role in T.A.'s shock syndrome. Id. at 472. He defined SIRS as systemic inflammatory response syndrome, reflecting a body-wide response to the release of cytokines. Id. at 474. There are varying degrees of SIRS. Id. at 475. Sepsis is bacterial infection in the bloodstream. Id. at 477. Viruses and fungi can cause cytokine storm. Id. at 477-78. In Dr. Whitton's view, it is a semantic issue. Id. at 478. He said, "I think of sepsis as bacterial, and I'm perfectly happy to accept a redesignation of sepsis to include other infections, but for me, the way I was trained, it's a bacterial infection entering the bloodstream." Id.

Dr. Whitton defined septic shock as when bacteria in the bloodstream, often called septicemia have caused sufficient stimulation of the innate immune response to trigger vast release of cytokines, both pro-inflammatory and anti-inflammatory, which leads to other signs and symptoms. Id. at 478-79. Bacterial septic shock is a type of cytokine storm. Id. at 479. The terms "sepsis," "septic shock," "SIRS," and "cytokine storm" overlap. Id. Dr. Whitton proceeded to draw a schematic (marked as Exhibit K). Id. at 482. He said that many bacterial infections exist in the absence of SIRS. Id. They do not trigger much of an immune response. Sometimes bacterial infections become a little bit more severe, and they begin to enter the domain of SIRS. Id. Some bacteria enter the bloodstream and this is sepsis. Id. at 483. Some move on to severe sepsis and some move on to septic shock. Id. All SIRS means is systemic inflammatory response which does not say anything about the clinical severity of that response. Id. Dr. Whitton prefers to talk about mild SIRS and severe SIRS and then SIRS shock. Id. at 484. One could get SIRS shock from nonbacterial causes and this means not all SIRS shock would be septic shock. Id.

Dr. Whitton moved on to viruses. Id. Many viruses do not cause even mild SIRS, but "a bunch of them" do. Id. Some viruses move into the mild SIRS category. Some viruses go out to cause septic shock, but this is semantics. The viruses cause what Dr. Whitton would call cytokine storm, but he has no objection whatsoever to calling it septic shock or virus-induced shock or SIRS shock. Id. But, he explained, "[H]ere we see that there is not a precise equivalence between SIRS shock and septic shock because if you have a SIRS shock caused by virus, it's not septic shock." Id. at 484-85. SIRS shock is the umbrella term Dr. Whitton would use. Id. at 485. He would "happily" also use cytokine storm because the two terms are basically synonymous. Id. All septic shock is SIRS shock. Id.

Dr. Whitton did not put measles vaccine on his chart. Id. He said that vaccines do not always induce SIRS, but they can certainly induce mild SIRS. Id. at 486. He stated, "I contend that vaccines do not induce SIRS shock or cytokine storm." Id. He knows of no literature to show that vaccines can induce cytokine storm. He says it is very difficult to understand how a vaccine could induce a shock syndrome. With MMR vaccine, Dr. Whitton sees no possible

biological reason to suspect it caused the catastrophically severe symptoms T.A. suffered. Id. He is basing his opinion on 30 years of knowledge and the medical literature. Id. Dr. Whitton said he has never worked with humans, but routinely vaccinates animals. Id. at 488. He stated vaccination induces the protective component of memory lymphocytes, part of the adaptive immune system. He also relies on literature but the literature petitioners filed on behalf of their experts does not suggest vaccines can cause shock. Id. Vaccines can cause fever, a bit of tachycardia, which would put the vaccinee in the mild SIRS category. Id. at 489.

Respondent's counsel asked Dr. Whitton if the chapter on shock from NELSON TEXTBOOK OF PEDIATRICS (Ex. B, Tab 3), "provide[d] a mechanism or state[d] that vaccines could cause cytokine storm" to which Dr. Whitton replied he did not recall. Id. at 491-92. Respondent's counsel then asked him whether the same chapter stated vaccines could cause severe SIRS or septic shock to which Dr. Whitton replied "certainly not severe SIRS or septic shock because I'm not aware of any evidence that they do." Id. at 492. [Table 64-5 on page 6 of Ex. B, Tab 3, is replicated in part earlier in this decision.]

Dr. Whitton then discussed how the immune system reacts to a bacteria. Id. Components of the bacterium called pathogen-associated molecular patterns ("PAMPS") activate the innate immune response. Id. Two of the common activators that bacteria carry which very strongly and explosively activate the innate immune response are a sugary lipid called lipopolysaccharide ("LPS") or endotoxin. Id. at 492-93. The innate immune system comprises a lot of different sensors that have a degree of specificity. Id. at 493. Either the LPS or endotoxin interact with a sensor. Id. One group of sensors is called the toll-like receptor of which there are 11 or 13. Bacterial endotoxin triggers toll-like receptor 4 ("TLR4"). Not all bacteria carries an endotoxin, but *Streptococcus pneumoniae* and *Neisseria meningitidis* do carry endotoxin. Id. The molecules combine with a signal through TLR4 and cause an explosive innate immune response with the production of cytokines. Id. Bacteria contain a second danger signal which is their DNA, although not all viruses and all bacteria contain DNA. Bacterial DNA differs from human DNA. Id. Bacterial DNA contains a higher proportion of CpG motifs. Id. at 493-94. Another of the TLRs, i.e., TLR9, has evolved to recognize DNA containing CpG motifs. Id. at 494. If a bacterium with endotoxin infects a person and causes septicemia, the innate immune system profoundly activates through TLR4 with endotoxin and TLR9 with bacterial DNA. Id.

Subsequently the adaptive immune system steps in and responds. Its response to bacteria differs from its response to viruses. The immune system responds to bacteria by activating B-lymphocytes which produce antibodies but also one subset of T-cells called CDR4-positive T-cells. Id. The innate immune response is dose-dependent in that a lot of bacteria produce a stronger response. The adaptive immune response is only dose-dependent until a threshold is reached and then it is activated. Id. at 496.

Viruses are similar in that the innate immune system contributes toll-like receptors and sensor molecules that are different than with bacteria. The innate response usually lasts for three to five days and then transits into the developing adaptive response which actually begins about day three but is so small, it is hard to detect. Id. By day 14, the adaptive begins to decline to

enter the memory phase which provides protective immunity. Id. at 497.

Another profound difference between viruses and bacteria is in the adaptive response because the adaptive response to viruses not only includes B-cells and CD4 T-cells, which collaborate to produce antibodies, but also very strong CD8-positive T-cells, which are very important for controlling viruses. Id. Dr. Whitton said the immune response is not monolithic. It responds differently to viruses and bacteria. Id. Genetic deficiencies of the immune system respond differently to bacteria than to viruses. Id. at 498.

When bacteria invade a host, triggering an innate immune response and its sensors, including mainly TLR4 and TLR9, cytokine storm can occur. Id. Some bacteria encode very specialized molecules called superantigens. Id. at 499. Superantigens act through the adaptive immune system, not through the innate immune system. Id. The adaptive immune system is highly specific. Id. at 500. If influenza or measles enters, it triggers maybe 100-200 of 10 million cells that are able to respond to that specific antigen. Id. This takes a matter of days to develop. Id. at 501. The reason it takes the adaptive immune response time to develop is it starts at a very low number of specific cells and takes about a week or two to develop the full complement of flu- or measles-specific cells. Id. By the end of 14 days after infection, the host has multiplied those 100-200 cells about 15-16 times and they begin to die, leaving memory cells which are the cornerstone of vaccination. That is the normal adaptive immune response. Id.

Dr. Whitton said there is no evidence that that can cause cytokine storm. But superantigens can act on these cells to cause cytokine storm. Superantigens do not active T-cells in a specific manner. They activate T-cells in a fairly nonspecific manner. Staphylococcal superantigen binds to molecules on the surface of T-cells and activates 10-15 percent of all T-cells, which is a large number. Id. Dr. Whitton said bacteria can induce a very rapid cytokine storm by this mechanism, the key to which is its rapidity. Id. at 502. With endotoxins, cytokine storm evolves rapidly because of stimulation of the innate immune system. Id.

Dr. Whitton said there is no evidence that MMR vaccine contains a superantigen. Even if it did, the vaccine would have triggered cytokine shock within two or three days not weeks later. Id. The innate immune system gets triggered within minutes but not noticeably until a few hours. Id. at 503. In a bacterial infection, if someone administers Rocephin, it acts very quickly to stop bacterial replication. Id. at 504. Even if the antibiotic kills the bacteria, the bacteria's DNA remains. Id. at 505. DNA can stimulate the innate immune response through CpG motifs. Id. The spleen clears membranes of the bacteria in 24-36 hours. Id.

Dr. Whitton stated that superantigens do not trigger the innate immune response; they inappropriately trigger the adaptive immune response. Id. at 507. Viruses differ in their capacity to trigger the innate immune response. Id. at 512. A superantigen would impact the adaptive immune system while an endotoxin would impact the innate immune system. Id. at 513. MMR does not contain a superantigen. Id. at 514.

The undersigned asked petitioners' immunologic expert Dr. Levin if he agreed with Dr.

Whitton's statement that only a superantigen can impact the adaptive immune system but MMR does not contain a superantigen. Id. at 515-16. Dr. Levin stated that Dr. Whitton was incorrect. Id. at 516. Medical literature describes cytokine storm involving a monoclonal antibody, not a superantigen, which affected the adaptive immune system causing a cytokine storm. Id. Dr. Whitton responded not only a superantigen but some drugs such as monoclonal antibodies can activate the adaptive immune system. Id. at 518.

Dr. Whitton stated that vaccines always cause a release of cytokines in the innate immune system. Id. at 519. Attenuated live viral vaccines cause an innate immune response although quantitatively probably a little bit less than wild viruses because they replicate much less than wild-type and there is less of the viral DNA or RNA to start triggering the innate response. Id. at 520. There are two purposes for the cytokines. The innate immune response to live viruses largely rests upon release of molecules called interferons, because they interfere with virus infection. These interferons act upon neighboring uninfected cells to alert them to the coming virus and these cells alter their physiology to make them more resistant to the viral infection. The other task of cytokines is to facilitate the development of the adaptive immune response. Id. The innate immune system cytokines last three to five days in mice. Id. As the adaptive immune response increases in cell numbers, those cells will make cytokine if they encounter viral antigen. Id. at 522. How long the adaptive immune response lasts depends on the type of viral infection. Id. at 523.

With MMR vaccine, the host has a primary infection. Id. at 524. Dr. Whitton stated, "I have no objection to the notion that the adaptive immune response to MMR in this specific case was occurring at around the time that T.A. developed his signs and symptoms. . . ." Id. at 527. Dr. Whitton thought that T.A.'s pediatrician Dr. Allen's opinion that T.A.'s petechiae, lethargy, and fever could be due to a bacterial infection or to an MMR reaction was reasonable. Id. at 527-28. T.A.'s loss of platelets was due to sepsis, septic shock, and DIC rather than due to MMR vaccine. Id. at 528. Dr. Whitton said that an injected throat (as T.A. had on August 24, 2011) "is certainly part of measles." Id. at 529. He did not think that T.A.'s injected throat was due to MMR vaccine because T.A. did not have Koplik spots. Id. at 529-30. Dr. Whitton said that T.A. had petechial hemorrhages and stated, "Unquestionably, MMR can cause petechial hemorrhages." Id. at 530. MMR can cause fever and T.A. had fever. Id. at 531. He thinks what happened to T.A. afterwards was due to a bacterial infection. Id. In his view T.A. had a normal adaptive immune response to MMR because it was the correct time frame. Id. at 533.

Dr. Whitton said that meningococcemia would have caused a fever, DIC, thrombocytopenia, and a spike in neutrophils. Id. at 535. He said the Rocephin did its job by killing the bacteria which maybe explains why it was not detectable. Id. But Rocephin does not remove the materials which stimulate the innate immune system. Id. The following colloquy occurred:

> THE COURT: Now, if he [T.A.] had a bacterial infection that brought him to the – to Dr. Allen on August 24th, 2011, why was his white count normal? It was only 6000 on August 24th, 2011.

> THE WITNESS: I confess, I am surprised by that. I would have expected an earlier elevation in his white count. . . . I'm surprised by that.

Id. at 536.

Dr. Whitton attributed all the catastrophic events that ensued from this date to T.A.'s innate immune response and not to his adaptive immune response. Id. at 539. He called it septic shock, or SIRS shock, or cytokine storm. Id. Dr. Whitton stated, "I almost cannot comment on whether or not there was an adaptive immune response. There may have been." Id. at 540. Dr. Whitton said that, possibly, T.A. did not mount an adaptive immune response because he received IVIG and steroids which suppress the immune response, but he also stated the suppressive response would tend to limit T.A.'s capacity to mount an adaptive response. Id. at 540-41. Dr. Whitton thinks a bacterium entered T.A. around seven days before the onset of his symptoms. Id. at 543.

Dr. Whitton, in responding to the Table time onset of 5-15 days for encephalopathy after MMR vaccine or 7-30 days for thrombocytopenia after MMR vaccine, said those intervals reflect the adaptive immune response to MMR vaccine. Id. at 548. He is unaware that a normal adaptive immune response ever causes cytokine storm. Id. at 549.

Dr. Whitton testified that there were two overlapping immune responses occurring at the time T.A. became sick. First was T.A.'s normal adaptive immune response to measles vaccine. Second was his innate immune response to the bacterium *Neisseria meningitidis*, causing cytokine storm and disseminated intravascular coagulation, which caused thrombocytopenia. Id. at 551. Dr. Whitton said he could not identify the biological infection T.A. had because it was not identified. Id. at 552. But he said T.A.'s symptoms were consistent with *Neisseria meningitidis*, particularly the petechiae and macular rash. Id. Respondent's counsel asked Dr. Whitton by what day after August 11, 2011 when T.A. received MMR vaccine would T.A.'s innate immune system have returned to normal. Id. at 554. Dr. Whitton responded, "Probably four or five days post-vaccination, somewhere around there." Id. He said cytokine storms can occur in the absence of an increase in neutrophils. Id. Neutrophils are generally a response to bacterial infection, not viral infection. Id. at 555. One can have cytokine storm without an elevation of neutrophils. Id. at 558. On August 24, 2011, T.A.'s absolute neutrophil count was 4.39, a normal value. Id. at 561. But on August 25, 2011, T.A.'s absolute neutrophil count rose to 15.11. Id.

The following colloquy occurred:

> THE COURT: [T]here may have been immune modulation from the two antigenic attacks at the same time. You could say four, because the measles/mumps/rubella—

> THE WITNESS: Yeah.
>
> THE COURT: -- vaccine is three antigens. So, you've got three attenuated live viral antigens working on the immune system to produce a response, while he's also fighting off a bacterial infection that's trying to provoke another response, and the immune system is not going – when it's got too much to deal with, it may not deal appropriately and neutrally with the bacterial attack. Is that consistent with your answer?
>
> THE WITNESS: I – I cannot exclude that possibility. I think it's an interesting suggestion.

Id. at 567. Respondent's counsel asked Dr. Whitton if he was aware of reliable evidence to support the conclusion that that was more likely than not, to which Dr. Whitton replied, "No." Id.

Dr. Whitton said if someone had a mild reaction to measles vaccine, he would not require Koplik spots. Id. at 574. Dr. Whitton said he believed in Occam's razor, that is, if there might be two explanations for something, it is better to have one explanation because it is simple. Id. at 576. That is why he attributes all of T.A.'s symptoms to *Neisseria meningitidis*. Id. He looked up the incubation period of meningococcus and it is two to ten days. Id. at 577. Usually, it is three to four days. Id. at 578.

Dr. Whitton said that antigen does not drive the adaptive immune response. Id. at 594. It triggers it. Id. The innate immune system feeds cytokines to the adaptive immune system to facilitate the development of the adaptive immune system. Id. at 595. Dr. Whitton stated that MMR vaccine does replicate, and this is an infectious process. Id. at 607. He admitted that the immune response to a live attenuated vaccine is similar to that produced by a natural infection. Id. at 608. He said that as the incoming genetic material in the vaccine virus replicates, the amount of viral RNA increases and provides a stronger trigger to the innate immune system. Id. at 614. The replication of this virus is extraordinarily limited, amounting to only about 20 times compared to thousands of times for the wild virus. Id. The tripping of the innate immune system would be more likely as the abundance of viral RNA continues to increase due to replication. Id. at 615. A twelve-day onset to symptoms such as fever and thrombocytopenia after MMR vaccination is a "perfectly reasonable" time frame to assume a vaccine reaction has occurred. Id. at 618. The following colloquy occurred:

> MR. DOWNING: I am at Exhibit B, Tab 3, page 6. . . . [D]oes Table 64.5 list a large grouping of differential possibilities for systemic inflammatory response syndrome?
>
> DR. WHITTON: It does.

> MR. DOWNING: Is measles [vaccine] listed as one of the potential infectious causes of systemic inflammatory response syndrome?
>
> DR. WHITTON: It is, and so it should be.

Id. at 619-20.

Dr. Whitton said that shock syndrome is undoubtedly attributable to cytokines without question. Id. at 635. Dr. Whitton denied that MMR vaccine can get the immune system to that level. Id. Dr. Whitton said he was not sure that MMR vaccine can cause encephalopathy even though HHS considers it a Table injury. Id. at 639. He said he does not know what the primary cause of measles encephalopathy is. Id. He said he does not know what the underlying biological mechanism of measles encephalopathy is. Id. at 640.

Petitioners' counsel then asked Dr. Whitton if T.A.'s illness satisfied the criteria in Table 64-7 of the chapter on shock [replicated earlier in this decision] from NELSON TEXTBOOK ON PEDIATRICS (Ex. B, Tab 3). Id. at 643. The heading of Table 64-7 is "International Consensus Definitions for Pediatric Sepsis." It has a left-hand column proceeding from infection → systemic inflammatory response syndrome (SIRS) → sepsis → severe sepsis → septic shock → multiple organ dysfunction syndrome. Next to each level are definitions of each category. In the category of SIRS, petitioners' counsel asked Dr. Whitton since T.A. had fever, tachycardia, respiratory distress, and leukocytosis, can we skip sepsis, severe sepsis, and septic shock because there was no infection and end up at multiple organ dysfunction syndrome. Id. at 644. Dr. Whitton replied, "Absolutely" and offered to explain why. Id. He said there are noninfectious causes of shock. Id. at 645. Dr. Whitton said someone could absolutely end up in MODS by skipping sepsis and severe sepsis in pancreatitis or trauma. Id. at 646. Dr. Whitton agreed that on August 25, 2011, T.A. had SIRS according to the definition of Table 64-7. Id. at 648. But he said T.A.'s extensive illness was not caused by MMR vaccine. Id. Dr. Whitton said T.A. developed shock. Id. Dr. Whitton admitted that MODS involves a lot of the same problems reflected under severe sepsis such as loss of cardiovascular integrity. Id. at 650. Dr. Whitton said T.A. had a suspected infection, but Dr. Whitton does not mean this was MMR infection because that virus would not be there anymore. Id. at 651, 683. He said he was talking about the bacterial infection that T.A. almost certainly had. Id. at 651.

T.A. had culture-negative sepsis. Id. at 669. Dr. Whitton admitted someone could have elevated neutrophils and SIRS without an infection. Id. at 677. Elevated levels of neutrophils are more likely produced in the context of bacterial infection rather than viral infection because neutrophils do not play a key role in clearing a virus. Id. at 677. He said lymphopenia (lowering the number of lymphocytes) is not unusual when there is ongoing profound inflammation. Id. at 680. Dr. Whitton said that cytokines can drive down leukocytes or lymphopenia. Id. at 682. Replication of MMR vaccine virus would occur in the first 72 hours. Id. at 684. Dr. Whitton believes that T.A.'s lethargy and fever resulted from bacterial stimulation of his innate immune response which subsequently developed into septic shock. Id. at 695. Dr. Whitton said "there's

no rational biological explanation for the vaccine having . . . trigger[ed] the cytokine storm." Id. at 697. T.A.'s fever showed his immune system was beginning to respond to a bacterial infection which progressed very rapidly. Id. The fever represented the very early stage of the innate response to bacterial lipopolysaccharide. Id. at 698. Dr. Whitton thinks the same events would have occurred even if T.A. had not received MMR vaccine. Id. at 704. He called measles vaccine a "crippled virus." Id. He thinks it unlikely that the adaptive immune response to MMR vaccine was going to interfere in any way with T.A.'s antibacterial response mainly because he did not have "a stunningly strong measles virus infection." Id.

Dr. Jerome Klein testified next for respondent. Id. at 718. He has been professor of pediatrics at the Boston University School of Medicine since 1974. Id. at 719. He is board-certified in pediatrics and consults in pediatric infectious diseases. Id. at 720-21. He has been teaching pediatric infectious disease since 1961. Id. at 722. He is an associate editor of *Clinical Infectious Diseases*, which he described as the most important infectious disease journal in the U.S. Id. at 724. Dr. Klein stopped seeing patients in 2010. Id. at 726.

In Dr. Klein's over 50-year practice, he would see two to three patients each year with bacterial sepsis. Id. at 728. The most challenging were those with meningococcal infections. Id. Some patients progressed to septic shock, particularly those with meningococcemia. Id. His opinion in this case is that T.A. suffered a catastrophic complication of meningococcal infection. Id. at 731. One of the bases of his opinion is that the Arkansas Children's Hospital physicians diagnosed T.A. with sepsis, septic shock, and meningococcemia based on all the information available to them, and managed T.A. as a meningococcemia case. Id. at 732. Another basis of his opinion is his own clinical experience. He has seen "this tragic circumstance a number of occasions." Id. In addition, the clinical and laboratory signs point to meningococcemia. Lastly, the lack of a microbiological diagnosis is readily explainable. Id.

Dr. Klein said that meningococcal colonization of the upper respiratory tract is relatively common. Id. at 733. T.A. was probably infected days before the parents noted he was tired on August 22, 2011. Id. at 734. As the organisms proliferated in the upper respiratory tract, at some point, they invaded T.A.'s blood. On August 23, 2011, he was febrile and sleeping most of the day, probably indicative of a systemic infection. Id. On August 24, 2011, T.A. had a petechial rash and a decreased platelet count of 97,000. Id. Normal platelet count would have been 150,000. Id. at 735. Dr. Allen gave T.A. 750 mg of ceftriaxone intramuscularly because he was concerned about a systemic bacterial infection. Id. Ceftriaxone is a cephalosporin antibiotic introduced in the 1990s and used against common bacterial organisms responsible for pediatric and adult diseases, including pneumococcus, streptococcus, staphylococcus, and meningococcus. Id. Dr. Klein said the unique feature of ceftriaxone was its long half-life. A dose would promote substantial antibacterial activity for more than 24 hours. However, Dr. Allen should have taken a culture of blood prior to administering ceftriaxone to T.A. Id. A blood culture would guide further management because it would be either positive the next day or negative and, then, the doctor would know this was not a systemic bacterial infection. Id. at 735-36. All the blood cultures that Arkansas Children's Hospital did were negative. Id. at 736. The hospital did PCR for other organisms, which were negative, but did not do PCR for meningococcal infection. Id.

T.A.'s petechial rash was an alarming feature because it may indicate bacterial invasive disease causing those hemorrhages in the skin. Id. at 739. This could be due not only to meningococcus, but also to pneumococcus, staphylococcus, and group A streptococcus. In addition, T.A. had a macular rash on his trunk. Id. Macules are discrete, small, red rashes. The typical rash of measles is called morbilliform rash, a blotchy rash which is not small maculars, but very extensive. Id. By the evening of August 24, 2011, T.A. had a higher temperature of 103 degrees and was vomiting and had diarrhea. Id. at 740. T.A. was toxic. He had significant fluid losses, what Dr. Allen described as 10 percent. Dr. Klein said that 10 percent is huge on the spectrum of dehydration. T.A. needed intravenous fluids and hospitalization. Id.

By August 25, 2011, T.A. was sufficiently ill so that Dr. Allen sent him to Mercy Hospital where he received another dose of ceftriaxone plus doxycycline. He was in severe respiratory distress and his oxygen saturations declined to 80, necessitating his being put on a ventilator. That evening, between 8:00 and 10:00 p.m., he was transferred to Arkansas Children's Hospital. Id.

Dr. Klein traced the trajectory of the disease from multiplying in the upper respiratory tract for the first three or four days and then, for unknown reasons, invading T.A.'s bloodstream. Id. at 741. Meningococcus has toxins that are responsible for stimulating white cells, including macrophages, monocytes, and lymphocytes to produce cytokines resulting in SIRS syndrome. Doctors use ceftriaxone to sterilize the blood but at the same time the antibiotic is killing the organism, it is also breaking open the envelope, releasing endotoxins. Id. The toxins then flood the system, releasing a burst of cytotoxins which is what happened to T.A. after he received ceftriaxone on August 24, 2011. Id.

T.A.'s white cell count was initially 6,000 on August 24, 2011 and then the infection stimulated the bone marrow to release more white cells, particularly neutrophils, so that on August 25, 2011, the total number of white blood cells was 20,000. Id. at 742. T.A.'s platelets were being consumed. His platelets in the peripheral blood decreased from 97,000 on August 24, 2011 to 73,000 on August 25th, both times at Dr. Allen's office, to 27,000 when he was at Arkansas Children's Hospital. Id. T.A. had disseminated (widespread) intravascular (within blood vessels) coagulopathy (clotting problem) or DIC. Id. at 742-43. The clotting may progress to complete obstruction of the arteries. Id. at 743. Since there is no blood going through the distal extremities (the feet, the hands), there is the potential for gangrene, which causes those tissues to die. Id. at 743. This is a recognized part of meningococcemia which Dr. Klein has seen on multiple occasions. Id. Usually capillary refill occurs in three seconds, but here it took more than six seconds. Id. at 744.

T.A. was in great distress, transferred to Arkansas Children's Hospital, and managed as a patient in septic shock with multisystem manifestations, including: renal failure, resulting in dialysis; respiratory failure, resulting in ventilation support; and the dreaded complication of DIC. Id. Dr. Klein said T.A.'s disease progression was a well-recognized complication of meningococcal infection. Id.

Dr. Klein said the five strains of meningococcus can be cultured, but T.A. received prior antibiotics before cultures were done and the culture of other fluids such as spinal fluid would have had to be done. Id. at 745. Because T.A. had coagulopathy and decreased platelets, the doctors were concerned about bleeding with a needle stick into his spinal fluid and, thus, T.A. did not receive a lumbar puncture. Id. Dr. Klein said he was "hypothesizing that [T.A.] had meningococcemia when he received the Rocephin on the 24th and that the blood culture that was taken on the 25th was negative." Id. When T.A.'s blood was cultured, the meningococcus was no longer available to be isolated. Id.

Dr. Klein's opinion is that MMR vaccine had nothing to do with T.A.'s disease, but he would not recommend that T.A. receive a second MMR vaccination because of the parents' anxiety over their associating his first MMR with his devastating event. Id. at 746. Dr. Klein regards the information about MMR being responsible for this sepsis event as speculative, but he is "almost certain" that T.A. had a tragic consequence as a complication of meningococcemia. Id. at 747. Dr. Klein said he has never heard and cannot find any medical literature to cause him to believe that a vaccine could cause septic shock and amputations. Id.

Dr. Klein said that the onset of T.A.'s meningococcal infection was August 22, 2011 when T.A.'s parents noted T.A. was not himself. Id. at 750. No PCR assay was done for meningococcal bacteria in T.A. Id. at 756. Dr. Klein described Arkansas Children's Hospital as a very highly progressive institution and Dr. Klein knows the infectious disease director there. Dr. Klein imagines that the staff had reasons not to do PCR testing and the PCR test availability was probably limited at the hospital. Id. The staff was very complete in looking at a variety of organisms such as Ehrlichia and rickettsia and they identified none of them. Id. at 757.

As for Table 64-5 (Ex. B, Tab 3), the chapter on shock from NELSON TEXTBOOK OF PEDIATRICS, which Dr. Klein gave respondent to file into evidence, Dr. Klein said he had no idea why the authors of chapter 64 included measles vaccine as a cause of SIRS. Id. at 759. Dr. Klein said that NELSON TEXTBOOK OF PEDIATRICS was not an authoritative source. Id. at 760. He does not recall why he gave this chapter to respondent's counsel to file into evidence. He admitted he uses NELSON TEXTBOOK OF PEDIATRICS in teaching. Id. He stated NELSON TEXTBOOK OF PEDIATRICS is an excellent textbook but that does not mean everything in it "has been presented with sufficient evidence to provide those indications." Id. at 761. He thinks the editors of this text "missed" and the reference to measles vaccine in the chapter on shock "was included without any sufficient evidence to support it." Id. Dr. Klein's opinion is that the chapter is right on all the other infectious causes the authors list except vaccinations. Id. at 763. Dr. Klein regards Table 64-5 as a "salad" with things that do not belong in that salad. Id.

Dr. Klein said that on August 24, 2011, T.A. was bacteremic, that is, the organism had invaded his blood. Id. at 771. T.A.'s petechial rash was due to the organism lodging in small blood vessels, producing a hemorrhage. Id. at 772. T.A.'s white blood cell count on August 24, 2011 was not elevated because the organism was in the process of stimulating T.A.'s bone marrow to produce more white blood cells, particularly neutrophils, which showed up in testing

on August 25, 2011. Id. at 772-73. Dr. Klein said he agreed with Dr. Whitton that SIRS is a spectrum. Id. at 782. Dr. Klein said he was quite confident that T.A. had meningococcemia with unfortunate complications that led to amputation. Id. at 784.

DISCUSSION

To satisfy their burden of proving causation in fact, petitioners must prove by preponderant evidence: "(1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury." Althen v. Sec'y of HHS, 418 F.3d 1274, 1278 (Fed. Cir. 2005). In Althen, the Federal Circuit quoted its opinion in Grant v. Secretary of Health and Human Services, 956 F.2d 1144, 1148 (Fed. Cir. 1992):

> A persuasive medical theory is demonstrated by "proof of a logical sequence of cause of and effect showing that the vaccination was the reason for the injury [,]" the logical sequence being supported by a "reputable medical or scientific explanation[,]" i.e., "evidence in the form of scientific studies or expert medical testimony[.]"

418 F.3d at 1278.

Without more, "evidence showing an absence of other causes does not meet petitioner's affirmative duty to show actual or legal causation." Grant, 956 F.2d at 1149. Mere temporal association is not sufficient to prove causation in fact. Id. at 1148.

Petitioners must show not only that but for MMR vaccine, T.A. would not have had SIRS and the complications leading to amputation of T.A.'s legs, but also that MMR vaccine was a substantial factor in causing T.A.'s SIRS and the complications leading to amputation of T.A.'s legs. Shyface v. Sec'y of HHS, 165 F.3d 1344, 1352 (Fed. Cir. 1999).

Change in Focus on the Issues in this Case

The undersigned's March 4, 2016 Order described the change in focus to petitioners' three assertions: (1) on-Table encephalopathy; (2) on-Table thrombocytopenic purpura; and (3) causation in fact SIRS. Respondent defends, asserting that petitioners do not satisfy the Qualifications and Aids to Interpretation ("QAI") for the Vaccine Injury Table for their two on-Table allegations, and that there is a known factor unrelated to the MMR vaccine, i.e., bacterial infection, which was the cause in fact of T.A.'s SIRS, shock, and bilateral amputation of his legs, as well as other injuries. Petitioners defend against respondent's claim of a known factor unrelated to the MMR vaccine by stating that test results were negative for any bacterial infection. Therefore, petitioners assert, respondent cannot satisfy his burden of proving there was a known factor unrelated to the administration of the vaccine that caused T.A.'s SIRS, shock, and bilateral amputation of his legs, as well as other injuries. Respondent counters

petitioners' defense by asserting that T.A.'s clinical symptoms (fever, petechiae, encephalopathy, thrombocytopenia, and shock) are classic for bacterial infection, specifically meningococcus, and although measles vaccine can cause a mild form of SIRS, it has never been known to be so severe as to cause shock.

On-Table Encephalopathy

The QAI for an on-Table encephalopathy require a vaccinee to have an acute encephalopathy for at least 24 hours. For someone older than 18 months of age, the QAI require, among other things, that a vaccinee's significantly decreased level of consciousness not be attributed to the effects of medication, such as sedation. 42 C.F.R. § 100.3(c)(2)(i)(B).[60]

T.A. received his first MMR vaccination on August 11, 2011. He again saw his pediatrician, Dr. L. Barry Allen, on August 23, 2011, at which time, he was not acutely encephalopathic. When he returned to Dr. Allen on August 24, 2011, he was much worse, transferred by ambulance to Mercy Hospital, and sedated by 4:25 p.m. Sedation affects one's level of consciousness. In order to have an on-Table encephalopathy between days five and 15 (the Table time interval) following MMR vaccination on August 11, 2011, T.A. would have had to have the onset of his acute encephalopathy no later than 4:24 p.m. on August 23, 2011. Since T.A. was consistently sedated for days after 4:25 p.m. on August 24, 2011, the only greater-than-24-hour period required to satisfy the on-Table encephalopathy QAI would have had to have occurred between August 23 and 24, 2011. Petitioners have not presented evidence that T.A. had an acute encephalopathy by 4:24 p.m. on August 23, 2011. Thus, petitioners have not satisfied the QAI for an on-Table encephalopathy after MMR vaccination.

Because the undersigned finds petitioners have not proven an on-Table encephalopathy, the undersigned will not discuss the opinions of petitioners' expert neurologist Dr. Siegel and respondent's expert neurologist Dr. Brown regarding a Table encephalopathy. The undersigned notes that the issue of encephalitis momentarily surfaced in this case, but this is not a credible diagnosis as no medical record supports T.A.'s having encephalitis. There is one notation in Arkansas Children's Hospital that T.A. had meningitis, but the undersigned regards that as an inadvertent error since T.A. did not have meningitis.

On-Table Thrombocytopenic Purpura

The QAI for an on-Table thrombocytopenic purpura require that the thrombocytopenic purpura not be "associated with disseminated intravascular coagulation, as observed with bacterial and viral infections." 42 C.F.R. § 100.3(c)(7).[61] T.A. was consistently noted to have

[60] (2) *Encephalopathy.* (i) *Acute encephalopathy.* … (B) For adults and children 18 months of age or older, an acute encephalopathy is one that persists at least 24 hours and is characterized by at least two of the following: (1) A significant change in mental status that is not medication related (such as a confusional state, delirium, or psychosis); (2) A significantly decreased level of consciousness which is independent of a seizure and cannot be attributed to the effects of medication; and (3) A seizure associated with loss of consciousness.

[61] (7) *Thrombocytopenic purpura*. This term is defined by the presence of clinical manifestations, such as petechiae, significant bruising, or spontaneous bleeding, and by a serum platelet count less than 50,000/mm with normal red

disseminated intravascular coagulation ("DIC"). Petitioners assert that T.A. did not have either a bacterial or a wild viral infection and, therefore, this proscription is inapplicable to their case. However the wording of the QAI for an on-Table thrombocytopenic purpura does not link the DIC to a bacterial and viral infection as a prerequisite. The link is "as observed with bacterial and viral infections." Thus, because T.A. had DIC, petitioners have not satisfied the QAI for an on-Table thrombocytopenic purpura after MMR vaccination.

The Meaning of "Known" Factor Unrelated

Respondent defends with a known factor unrelated to vaccine of a bacterial infection, probably *Neisseria meningitidis*. Petitioners deny that T.A. had a bacterial infection because blood cultures, urine cultures, tissue stains, and PCR assays have all been negative. Respondent states that, based on clinical symptoms and course of disease, T.A. had the signs and symptoms of a bacterial SIRS, and numerous doctors at Arkansas Children's Hospital wrote that T.A. had a meningococcal infection or meningococcemia in the medical records. The determination of who is legally correct depends on an interpretation of 42 U.S.C. § 300aa-13(a)(2)(A) and (B). Petitioners' burden is to prove their allegations by a preponderance of the evidence. Section 300aa-13(a)(1)(A). If petitioners put on a prima facie case, the burden then shifts to respondent to show that the vaccinee's illness "is due to factors unrelated to the administration of the vaccine. . . ." Section 300aa-13(a)(1)(B).

The Vaccine Act further defines what are "factors unrelated to the administration of the vaccine." Section 300aa-13(a)(2). Factors unrelated to the vaccine do not include "any idiopathic, unexplained, unknown, hypothetical, or undocumentable cause . . . ." Section 300aa-13(a)(2)(A). Factors unrelated to the vaccine may include "infection, toxins, trauma . . ., or metabolic disturbances . . . ." Section 300aa-13(a)(2)(B).

Petitioners argue that § 300aa-13(a)(2)(A) applies in this case because all of the blood cultures, tissue stains, and PCR assays were negative for bacteria. Respondent argues that § 300aa-13(a)(2)(B) applies because clinical signs and symptoms and the course of the illness indicate that T.A. had a bacterial infection and, therefore, the factor unrelated to the MMR vaccine was not unexplained, unknown, or undocumentable. Dr. Jerome Klein, respondent's expert, relies on decades of experience as a pediatric infectious disease specialist in concluding T.A. had a bacterial SIRS. Dr. Whitton, respondent's immunologic expert, testified that this most likely was meningococcemia. He cannot imagine the specific biological mechanism to explain how MMR vaccine could cause multiorgan failure although he accepts that MMR vaccine can, and did, in this case cause T.A. to have SIRS.

Respondent's Argument that SIRS has to start immediately

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and white blood cell indices. Thrombocytopenic purpura does not include cases of thrombocytopenia associated with other causes such as hypersplenism, autoimmune disorders (including alloantibodies from previous transfusions) [,] myelodysplasias, lymphoproliferative disorders, congenital thrombocytopenia or hemolytic uremic syndrome. Thrombocytopenic purpura does not include cases of thrombocytopenia associated with disseminated intravascular coagulation, as observed with bacterial and viral infections.

Dr. Whitton and Dr. Klein stated that underlying SIRS is the heightened activity of cytokines which must happen immediately after the triggering event.

An analysis of respondent's own view as to when an immunologic reaction to MMR vaccine occurs is instructive. When formulating what should be the appropriate timing for a Table encephalopathy after MMR vaccination, respondent's view of onset changed from the inception of the Vaccine Program on October 1, 1988 until his first revision of the Vaccine Injury Table on February 8, 1995, effective March 10, 1995. Initially, the onset interval for a Table encephalopathy after MMR vaccine was 0-15 days. However, except in the case of anaphylaxis, after this first Table Revision in 1995, respondent required at least a five-day interval from vaccination to onset to have a Table encephalopathy. This change in on-Table onset after MMR vaccine from the original Table onset of 0-15 days to the revised Table onset of 5-15 days in the case of a Table encephalopathy was based on respondent's realization that viral replication of at least five days was necessary:

> Since viral replication is required for a viral vaccine-associated encephalopathy, a window for the expected time of onset is appropriate. The onset of vaccine-related illness following MMR (or any of its components) is generally from 7 to 14 days[;] thus a time interval of 5 to 15 days would be all-inclusive.

National Vaccine Injury Compensation Program Revision of the Vaccine Injury Table, 60 Fed. Reg. 7678, 7692 (Feb. 8. 1995, effective Mar. 10, 1995) (to be codified at 42 C.F.R. § 100.3(a)).

Thus, respondent recognizes that immunologically a Table encephalopathy is not going to constitute an adverse reaction to MMR vaccine if it occurs immediately after vaccination. As for SIRS, petitioners' filing of the medical article by Helfand, Timing of Development of Measles-Specific Immunoglobulin M and G after Primary Measles Vaccination (Ex. 44), showing that IgM mostly develops two to three weeks after MMR vaccination is support for Dr. Allen's and Dr. Levin's testimony that the onset of T.A.'s SIRS occurred at the most appropriate time post-vaccination to reflect an immunologic challenge. On his first day of testimony, Dr. Whitton thought it possible and an interesting suggestion that T.A. could have both an MMR-induced SIRS coupled with a bacterial infection, but on his second day of testimony, he rejected this suggestion and instead preferred the Occam's razor or "unity" theory, i.e., one explanation is much simpler and preferable to two explanations. The Federal Circuit, however, rejected the "unity" theory in Knudsen, 35 F.3d at 550 (in Knudsen, respondent said the baby had a cold which must have caused her encephalopathy under this "unity" theory, whereas the Federal Circuit saw no difficulty in holding that the baby had both a cold and a DPT-caused encephalopathy).

The point however for this decision is that respondent's expert Dr. Whitton accepts that SIRS is appropriate, even reasonable, 12 days after MMR vaccination. Dr. Whitton does not accept that T.A.'s MMR vaccine-induced SIRS, if he had it, led to shock, multiorgan dysfunction

syndrome, and bilateral amputation. The undersigned finds that the evidence and testimony best support the conclusion that SIRS does not have to occur immediately post-MMR vaccination, and that an onset nearly two weeks later is immunologically reasonable, as Dr. Whitton initially testified.

Respondent's Defense

Respondent has two defenses to petitioners' allegations of causation in fact from MMR vaccine: (1) although he admits that T.A. had SIRS, Dr. Whitton does not know the underlying biological mechanism to explain how MMR vaccine-caused SIRS led to the catastrophic condition T.A. experienced, ultimately necessitating amputation of his legs; and (2) neither Dr. Whitton nor Dr. Klein knows of any medical literature that supports petitioners' allegation that MMR vaccine-induced SIRS can lead to the catastrophic condition ultimately causing amputation of T.A.'s legs.

These defenses fail in light of the Federal Circuit's decisions in Knudsen v. Sec'y of HHS, 35 F.3d 543 (Fed. Cir. 1994), and Capizzano v. Sec'y of HHS, 440 F.3d 1317 (Fed. Cir. 2006). Petitioners do not have the burden of proving a specific biological mechanism or providing medical literature in support of their allegations:

As the Federal Circuit stated in Knudsen, 35 F.3d at 549:

> Furthermore, to require identification and proof of specific biological mechanisms would be inconsistent with the purpose and nature of the vaccine compensation program. The Vaccine Act does not contemplate full blown tort litigation in the Court of Federal Claims. The Vaccine Act established a federal "compensation program" under which awards are to be "made to vaccine-injured persons quickly, easily, and with certainty and generosity." House Report 99-908, supra, at 3, 1986 U.S.C.C.A.N. at 6344.
>
> The Court of Federal Claims is therefore not to be seen as a vehicle for ascertaining precisely how and why DTP and other vaccines sometimes destroy the health and lives of certain children while safely immunizing most others.

As the Federal Circuit stated in Capizzano, 440 F.3d at 1325:

> [W]e conclude that requiring either epidemiologic studies, rechallenge, the presence of pathological markers or genetic disposition, or general acceptance in the scientific or medical communities to establish a logical sequence of cause and effect is contrary to what we said in Althen . . . . We think such an approach is inconsistent with the use of circumstantial evidence.

> Id. The Federal Circuit stated in Althen, 418 F.3d at 1280, that "the purpose of the Vaccine Act's preponderance standard is to allow the finding of causation in a field bereft of complete and direct proof of how vaccines affect the human body."

The undersigned respects the sterling credentials of both Dr. Whitton and Dr. Klein. However, the undersigned finds that under the law as the Federal Circuit has interpreted it, their testimony does not vitiate petitioners' proof. Dr. Whitton not only denied that MMR vaccine-induced SIRS could lead to T.A.'s catastrophic illness because Dr. Whitton does not know what is the underlying biological mechanism, but also he denied the validity of respondent's including encephalopathy as a Table injury within 5-15 days of MMR vaccination because he does not know what is the underlying biological mechanism for MMR-induced encephalopathy. The undersigned finds his position opposing the Table injury of encephalopathy after MMR vaccination remarkable because HHS does not create a Table injury without scientific and medical input and HHS changed the Table onset for MMR vaccine encephalopathy from 0-15 days to 5-15 days based on scientific and medical input. See, e.g., 42 U.S.C. § 300aa-2(a)(7). **Evaluating the need for and the effectiveness and adverse effects of vaccines and immunization activities**:

> The Director of the Program shall, through the plan issued under section 300aa-3 of this title [preparation and issuance of a plan for the implementation of responsibilities; the plan shall establish priorities in research and the development, testing, licensing, production, procurement, distribution, and effective use of vaccines], coordinate and provide direction to the National Institutes of Health, the Centers for Disease Control and Prevention, the Office of Biologics Research and Review of the Food and Drug Administration, the National Center for Health Statistics, the National Center for Health Services Research and Health Care Technology Assessment, and the Health Care Financing Administration in monitoring the need for and the effectiveness and **adverse effects of vaccines** and immunization activities.

(emphasis added).

In addition, Dr. Whitton, as he frequently stated at the hearing, does not see medical patients. He is not a clinician in any specialty. He is not licensed to practice medicine in the United States. His extensive knowledge about immunology derives from animal research.

In contradistinction to Dr. Whitton's acceptance of measles vaccine as a cause of SIRS, Dr. Klein does not accept MMR vaccine as a cause of SIRS for two reasons: (1) the lack of medical literature to support that assertion, and (2) he has not seen patients with MMR vaccine-induced SIRS in his own clinical experience. But the Federal Circuit in Althen, 418 F.3d at

1280, states that requiring medical literature as part of petitioners' proof "contravenes section 300aa-13(a)(1)'s allowance of medical opinion as proof." The Federal Circuit in Capizzano, 440 F.3d at 549, states petitioners do not have to prove general acceptance in the scientific or medical communities. Moreover, a rare adverse reaction to a vaccine would be unlikely to appear in a clinician's practice.

Dr. Klein in his testimony disparaged the chapter on shock in NELSON TEXTBOOK OF PEDIATRICS, which lists measles vaccine as an infectious cause of SIRS, even denying the textbook is an authoritative source. But then, on cross-examination, Dr. Klein admitted he uses this very same textbook when he teaches. Dr. Klein undercut his own credibility. Dr. Levin, petitioners' expert immunologist, called NELSON TEXTBOOK OF PEDIATRICS the bible of pediatrics.

The undersigned finds Dr. Whitton's acceptance of measles vaccine as a cause of SIRS more credible than Dr. Klein's denial of measles vaccine as a cause of SIRS, particularly since the two authors of the chapter on shock are accomplished pediatricians involved in critical care medicine at Duke. These accomplished pediatricians are: (1) Dr. David A. Turner, Associate Director, Pediatric Critical Care Fellowship Program; Medical Instructor, Department of Pediatrics, Division of Pediatric Critical Care Medicine, at Duke University Medical Center, Durham, North Carolina, and (2) Dr. Ira M. Cheifetz, Professor of Pediatrics; Chief, Pediatric Critical Care Medicine; Medical Director, Pediatric ICU; Medical Director, Pediatric Respiratory Care & ECMO Programs, at Duke Children's Hospital, Durham, North Carolina. At the end of the chapter on shock, these co-authors offer to the reader a complete bibliography at www.expertconsult.com. Undoubtedly this website has changed since the 2011 date of publication of the 19th edition because it advertises the 20th edition which was published in 2016. The website states:

> After more than 75 years, Nelson Textbook of Pediatrics remains the indispensable source for definitive, state-of-the-art answers on all aspects of pediatric care. This classic reference provides essential information that practitioners and other care providers involved in pediatric health care need to understand to effectively address the enormous range of biologic, psychologic, and social problems that children and youths may face. Regular online updates personally selected by Dr. [Robert M.] Kliegman ensure that you have the most recent information on diagnosis and treatment of pediatric diseases based on the latest recommendations and methodologies.

https://expertconsult.inkling.com/store/book/kliegman-nelson-textbook-pediatrics-20/ (last visited August 8, 2018).

The undersigned notes that both Dr. Whitton and Dr. Klein explained the lack of a positive blood or urine culture detecting meningococcus based on their assumption that Dr.

Allen, T.A.'s pediatrician, administered Rocephin to T.A. before any cultures were done, and thus the antibiotic eliminated the successful detection of meningococcus. However, Dr. Allen told Dr. Joseph R. Romero, an infectious diseases consultant at Arkansas Children's Hospital, on August 26, 2011 that Dr. Allen had performed a blood culture, a nasopharyngeal swab, and a urine culture, all of which were negative, before he gave T.A. Rocephin on August 24, 2011.[62] Exhibit 7, at 473. If Dr. Whitton's and Dr. Klein's opinion that T.A. had meningococcemia or another bacterial infection were valid, one or all of those tests should have been positive. In fact, Dr. Klein emphasized that meningococcus resides in many people's nasal passages. He said he himself had a problem with meningococcus in his own nasal passages and developed petechiae which with medication became better. But when Dr. Allen did a nasopharyngeal swab of T.A.'s nasal passages, the result was negative, as were the blood and urine cultures prior to Dr. Allen's administration of Rocephin.

This contemporaneous medical record on August 26, 2011 reporting Dr. Allen's conversation with Dr. Romero just two days after Dr. Allen performed the blood culture, nasopharyngeal swab, and urine culture before administering Rocephin makes respondent's experts' explanation of the subsequent negative blood and urine cultures, as well as other tests, done at Mercy Hospital and Arkansas Children's Hospital not credible. The undersigned notes that Dr. Allen testified by telephone at the hearing and, when he was finished, hung up. He never got to hear Dr. Whitton's and Dr. Klein's testimony (and it is unclear if he ever read their expert reports) that the blood and urine cultures at Mercy Hospital and Arkansas Children's Hospital were negative because Dr. Allen had not performed any testing on T.A.'s blood, urine, or nasopharyngeal passages before administering Rocephin. The undersigned also reflects that some of the other medical doctors note in the Arkansas Children's Hospital records that, even though T.A. was repeatedly tested, the administration of Rocephin and other antibiotics was probably the cause of the negative test results. The undersigned assumes these busy doctors did not comb through T.A.'s voluminous hospital records to see if Dr. Allen had told a doctor in the hospital that Dr. Allen had administered Rocephin after he did a blood culture, nasopharyngeal swab, and urine culture.

Thus, respondent's known factor unrelated to MMR vaccine that T.A. had in fact

[62] The undersigned cannot find in the filing of Dr. Allen's pediatric records for August 24, 2011 that he noted the blood culture, nasopharyngeal swab, and urine culture or the actual test results on a different page than the pediatric notes for the visit of August 24, 2011. The undersigned however credits Dr. Allen's history to Dr. Romero because the undersigned has heard Dr. Allen testify and finds him eminently credible and is aware that sometimes medical record notes are incomplete and lab test results do not make their way into medical records that counsel files. Moreover, Dr. Allen would have had no idea that Dr. Romero was including in the hospital records the history Dr. Allen gave Dr. Romero since Dr. Romero dictated his notes later. Med. recs. Ex. 7, at 476. Since this was a conversation during an emergency admittance with a little boy's life on the line (and not in the context of litigation), Dr. Allen would have been motivated to give Dr. Romero every piece of information he could from T.A.'s visit two days earlier plus the day before that would help Dr. Romero treat this little boy. The undersigned is cognizant that on August 25, 2011, Dr. Allen cancelled all of his appointments that day in order to accompany T.A. to Mercy Hospital by ambulance, stayed with him throughout his stay there, and signed the Angel One Transport Medical Necessity Form to enable T.A. to proceed by helicopter to Arkansas Children's Hospital the night of August 25, 2011. Med. recs. Ex. 6, at 6. Since the conversation he had with Dr. Romero occurred on August 26, 2011, Dr. Allen must have driven to Arkansas Children's Hospital where he joined petitioners in speaking to Dr. Romero.

meningococcemia or another bacterial infection, undetected because of prior administration of antibiotics, which caused in fact his SIRS and its sequelae fails. Even if, however, Dr. Romero dictated his notes on August 26, 2011 incorrectly, i.e., Dr. Allen told him he did a blood culture, nasopharyngeal swab, and urine culture after not before he administered Rocephin to T.A., respondent's known factor unrelated to MMR vaccine fails because the numerous and varied antibiotics T.A. received did not improve his condition. The undersigned is convinced that the medical staff at Arkansas Children's Hospital diagnosed T.A. with meningococcemia because it is a well-accepted cause of SIRS, sepsis, septic shock, and multiorgan dysfunction syndrome and most, if not all, of the doctors were unaware that T.A. had received MMR vaccine almost two weeks before he became ill. Even if they had known of the preceding MMR vaccination, the rarity of this catastrophic reaction would have eliminated MMR vaccine as a cause from their minds, just as it did from Dr. Whitton's and Dr. Klein's minds. But the rarity of an occurrence does not mean it is non-existent.

Petitioners' Proof of Causation in Fact

Respondent filed two of the most important pieces of medical literature that benefit petitioners. The first is the chapter on shock in NELSON TEXTBOOK OF PEDIATRICS. The second is the Medscape article by Steven D. Burdette on SIRS, Systemic Inflammatory Response Syndrome (Ex. E, Tab 6), which states that SIRS is not always related to infection and that whatever the etiology of SIRS, it has the same pathophysiologic properties with minor differences in inciting cascades. The author states that inflammation is the body's response to nonspecific insults that can include a reaction to a drug. He also states both infectious and non-infectious SIRS have similar clinical characteristics. Although respondent filed Exhibit E, Tab 6, to Dr. Whitton's expert report, its conclusions undercut Dr. Whitton's testimony that MMR-induced SIRS can never be as severe as bacterial SIRS.

Petitioners filed an excerpt from a Centers for Disease Control and Prevention ("CDC") publication on prevention of vaccine-preventable diseases (Ex. 36) which states that the immune response to a live attenuated vaccine is virtually identical to the immune response to a natural infection because the immune system does not differentiate between an infection with an attenuated viral vaccine and a wild viral infection. The CDC is part of HHS. This publication undercuts the credibility of both Dr. Whitton and Dr. Klein, who insist that MMR vaccine can never cause the severe sequelae that happened to T.A., although Dr. Whitton concedes MMR vaccine can cause SIRS, but it will always be mild, and Dr. Klein denies that MMR vaccine can even cause SIRS.

Dr. Allen testified that he has had patients who had adverse reactions to MMR vaccine. He testified that he has thought about T.A. several times over the past years and he has to think MMR was the cause of T.A.'s illness in light of timing after vaccination and the failure of the cultures and PCR to find a bacterial cause. He said he would be very reluctant to recommend that T.A. receive a second MMR vaccination: "Well, that would be a very difficult decision for me. I would probably recommend the other immunizations, but I would be very reluctant to recommend an MMR for T.A." Tr. at 114. "A treating doctor's recommendation to withhold a

particular vaccination can provide probative evidence of a causal link between the vaccination and an injury a claimant has sustained." Andreu v. Sec'y of HHS, 569 F.3d 1367, 1376 (Fed. Cir. 2009 (citing Capizzano, 440 F.3d at 1320, 1326).

Dr. Levin, whom respondent accepted as an expert in immunology, testified based on the Helfand article, Timing of Development of Measles-Specific Immunoglobulin M and G after Primary Measles Vaccination (Ex. 44), showing that IgM mostly develops two to three weeks after MMR vaccination, that one would not expect an immunological response to a first MMR vaccination until at least a week or two weeks. He explained SIRS by saying that people have only a few ways of responding to an immunologic insult, and SIRS is a way people respond to bacteria, viruses, fungi, toxic chemicals, and vaccines. Once SIRS is triggered, it proceeds spontaneously as it did in T.A. He said there is an overreaction of pro-inflammatory or anti-inflammatory cytokines and other agents that cause an inflammatory response. In T.A.'s case, the pro-inflammatory cytokines caused the harm. T.A.'s maculopapular rash, petechial rash, 103-degree fever, vomiting, and diarrhea were consistent with a systemic reaction going out of control. Dr. Levin testified that MMR vaccine caused T.A.'s fever on August 23, 2011 due to pro-inflammatory cytokines. His white cell count rose from 6,000 to 20,000, a typical SIRS reaction to bacteria, viruses, toxic chemicals, and vaccines. The petechial rashes and little blood clots were due both to the decrease in platelet counts and to MMR vaccine. Titers were taken that showed T.A. was positive to measles. Dr. Levin noted that Rocephin, the antibiotic, did not work and T.A. became much sicker. Dr. Levin ascribes the failure of Rocephin to help T.A. as an indication that T.A. did not have a bacterial infection, noting that meningococcus is exquisitely sensitive to Rocephin. Dr. Levin called the immunology unit of Arkansas Children's Hospital one of the best in the country. He said the reason those doctors could not find a pathogen was probably because MMR vaccine caused T.A.'s SIRS. Dr. Levin said all SIRS is the same whether the trigger is bacterial or a vaccinal. This is because people have a limited repertory of responses to immunologic insults.

Considering the Opinions of Treating Physicians

The Federal Circuit in Capizzano, 440 F.3d at 1326, emphasized that the special masters are to evaluate seriously the opinions of petitioner's treating doctors since "treating physicians are likely to be in the best position to determine whether a logical sequence of cause and effect show[s] that the vaccination was the reason for the injury." See also Broekelschen v. Sec'y of HHS, 618 F.3d 1339, 1347 (Fed. Cir. 2010); Andreu v. Sec'y of HHS, 569 F.3d 1367, 1375 (Fed. Cir. 2009).

The undersigned takes seriously Dr. Allen's opinion that T.A. had an adverse reaction to MMR vaccination which led to his thrombocytopenia, necessitating amputation of T.A.'s legs. Dr. Allen is T.A.'s treating pediatrician who had 36 years of experience when the 2011 events occurred. When he testified, Dr. Allen had 40 years of experience as a pediatrician. The undersigned recognizes that initially Dr. Allen thought T.A. might have a bacterial infection which is why he initially gave T.A. Rocephin. The undersigned is also aware that the doctors at Mercy Hospital, where T.A. was initially taken, diagnosed him with sepsis, and the doctors at

Arkansas Children's Hospital diagnosed T.A. with sepsis, septic shock, or meningococcemia. The undersigned contrasts the time that Dr. Allen has had since 2011 to reflect on what caused T.A.'s illness versus the emergency situation prevailing at Mercy Hospital and Arkansas Children's Hospital where T.A. was on the verge of death. No doubt, the treaters at both hospitals saw more cases of sepsis and meningococcemia than of MMR vaccine-induced SIRS. That a reaction is rare does not mean it never occurs. As the Federal Circuit stated in Knudsen, 35 F.3d at 550:

> The bare statistical fact that there are more reported cases of viral encephalopathies than there are reported cases of DTP encephalopathies is not evidence that in a particular case an encephalopathy following a DTP vaccination was in fact caused by a viral infection present in the child and not caused by the DTP vaccine.

Moreover, if someone were to view Dr. Allen's opinion and the treating doctors' opinions at Mercy Hospital and Arkansas Children's Hospital as in equipoise, and thus cancel each other out, the Federal Circuit states that Congress, in passing the National Childhood Vaccine Injury Act, envisioned a system "in which close calls regarding causation are resolved in favor of injured claimants." Althen, 418 F.3d at 1280.

Althen Analysis

Prong One

The undersigned has narrowed the issues to one issue: can MMR vaccine cause SIRS followed by sequelae of shock and amputation. Based on the evidence submitted, the undersigned finds the answer is yes. Dr. Whitton, respondent's immunologic expert, accepts that measles vaccine can cause SIRS, although Dr. Klein, respondent's infectious diseases expert, denies that. However, Dr. Whitton denies that a MMR-vaccine-induced SIRS can lead to the sequelae of shock and multiorgan dysfunction syndrome. Petitioners' immunological expert Dr. Levin testified that MMR vaccine can cause on rare occasions SIRS leading to shock and multiorgan dysfunction syndrome.

The medical literature that respondent filed, particularly chapter 64 on shock from the 19th edition of NELSON TEXTBOOK OF PEDIATRICS, supports petitioners' allegation that MMR vaccine can cause SIRS. Respondent also filed an article from the online site Medscape by Steven D. Burdette on SIRS, Systemic Inflammatory Response Syndrome (Ex. E, Tab 6), that states that SIRS is not always related to infection and that whatever the etiology of a particular case of SIRS, SIRS has the same pathophysiologic properties with minor differences in inciting cascades. The author states that inflammation is the body's response to nonspecific insults that can include a reaction to a drug. He also states both infectious and non-infectious SIRS have similar clinical characteristics. Both these pieces of literature are consistent with petitioners' expert immunologist Dr. Levin's testimony.

Petitioners filed an excerpt from a CDC publication on prevention of vaccine-preventable diseases (Ex. 36) which states that the immune response to a live attenuated vaccine is virtually identical to the immune response to a natural infection because the immune system does not differentiate between an infection with an attenuated viral vaccine and a wild viral infection. This excerpt is consistent with petitioners' expert Dr. Levin's testimony.

The undersigned finds that as to Althen Prong One, petitioners' expert Dr. Levin is more credible than respondent's experts Dr. Whitton and Dr. Klein and that the medical literature supports Dr. Levin's testimony and refutes respondent's experts' testimony. The undersigned finds that MMR vaccine can on rare occasions cause SIRS, shock, and multiorgan dysfunction syndrome, leading to bilateral amputation.

Prong Two

Based on the undersigned's finding above for petitioners on Prong One and the discussion below finding for petitioners on Prong Three, the undersigned finds that petitioners have proved that MMR vaccine did cause in fact T.A.'s SIRS, shock, multiorgan dysfunction syndrome, and bilateral amputation based on the testimony of Dr. Levin and the medical literature described above in the discussion of Prong One.

Prong Three

The timing for an immune challenge (not including anaphylaxis) after MMR vaccine is one to two weeks, according to both HHS in its Table injury of encephalopathy, and two to three weeks according to the Helfand article, Timing of Development of Measles-Specific Immunoglobulin M and G after Primary Measles Vaccination (Ex. 44), showing that IgM mostly develops two to three weeks after MMR vaccination and that one would not expect an immunological response to a first MMR vaccination until at least a week or two weeks. T.A.'s onset of SIRS was on either August 23 or 24, 2011, that is, either 12 or 13 days after his MMR vaccination. The timing of his illness fits perfectly within the onset interval that doctors (including respondent's Dr. Whitton) would say is causally related to MMR vaccine. Dr. Levin relied on this article as support for his opinion that T.A.'s onset of SIRS, followed by shock and multiorgan dysfunction syndrome, was consistent with an immunologic challenge resulting in an adverse reaction.

Petitioners have successfully proved a prima facie case of causation in fact. Respondent has failed to satisfy the criteria for proving a known factor unrelated to MMR vaccine caused in fact T.A.'s SIRS, shock, multiorgan dysfunction syndrome, and bilateral amputation.

CONCLUSION

This is a tragic case involving a little boy who had an adverse reaction to MMR vaccine, including rash, fever, lethargy, and irritability 12 or 13 days later, a medically appropriate time

for such a reaction, and whose worsened condition resulted in SIRS, shock, multiorgan dysfunction syndrome, and bilateral amputation of his legs. Based on the evidence submitted and the testimony of the experts at the hearing, the undersigned rules that petitioners are entitled to compensation.

The undersigned encourages the parties to proceed diligently to settle damages. Petitioners merit $250,000.00 in pain and suffering. Petitioners must ascertain the amount of the Medicaid lien pertaining to T.A.'s illness and sequelae, and provide that information and documentation of unreimbursable medical expenses to respondent.

The undersigned will set a telephonic status conference soon to discuss how the parties are proceeding in settling damages.

IT IS SO ORDERED.

Dated: August 16, 2018

/s/ Laura D. Millman
Laura D. Millman
Special Master